The Decline of 'Deaths of Despair' in Italy: Unveiling This Phenomenon in a New Context

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Abstract

This paper explores the classification of "Deaths of Despair" (DoD), focusing on mortality due to alcohol consumption, drug use, and suicides. While the concept has been predominantly studied in the United States, where these deaths have increased significantly, this analysis applies it to Italy, which exhibits comparatively lower DoD rates. Utilizing ISTAT data from 1983 to 2018, aggregated by gender and age groups at the NUTS1 level, the study reveals a decline in DoD mortality in Italy, driven mainly by a reduction in alcohol-related deaths. The findings contrast with U.S. trends, particularly in the magnitude and trajectory of drug-related deaths, offering valuable insights into the unique dynamics of DoD in Italy. Through Cointegration Analysis, it was determined that there is no significant dependency structure between these causes or across regions, with only a few exceptions. These findings suggest that in Italy, DoD should not be treated as a homogenous group, but rather as distinct outcomes of despair that require separate consideration in public health analyses and interventions.

Keywords: Deaths-of-Despair; Causes-of-Deaths; Mortality; Italy; Alcohol; Drugs; Suicide;

1 Introduction

In the global longevity scenario, Italy has proven to be a potential competitor for leading positions in the evolution of life expectancy (Nigri et al. 2022*b*). Since the early 1960s, significant strides in reducing mortality have been central to Italy's improvement in longevity, considering that since 1900, the life expectancy of Italian women at birth has increased from 50 to 84.7 years, averaging a rise of 2.9 years per decade (Human Mortality Database 2024).

In the late 1970s, the Italian Government established the Italian National Health Service (SSN), founded on the principle of universal coverage. The SSN has since become a global model for healthcare systems. This investment has significantly contributed to the progress in Italian longevity, ensuring access to surgical procedures, medical care, prescription drugs, specialist consultations, and diagnostic tests for all citizens, regardless of income. It specifically provides comprehensive care for individuals with chronic diseases and for those aged 65 and above. Following the increase in life expectancy driven by advancements in early diagnoses, the diversification of diseases has significantly increased, thereby challenging the stability of healthcare systems. For instance, an exploratory analysis conducted in 2012 revealed that cardiovascular diseases accounted for 30% of all deaths, followed by malignant neoplasms of the trachea, bronchi, and lungs (ISTAT 2014).

Examining specific age groups, transportation-related accidents were the leading cause of death among individuals aged 15-24 years. For the age group of 65-84 years, this demographic represented approximately 50% of overall mortality, with ischemic heart diseases being the leading cause of death for males and cerebrovascular diseases for females. Among those aged 85 and above, diseases of the circulatory system, particularly heart diseases, were the most common causes of death (ISTAT 2014).

According to Nigri et al. (2022*b*), Italian public health policy could promote future increases in life expectancy by focusing on reducing cancer and cardiovascular diseases (CVD) for both sexes and mortality from external causes for men. The reduction in cardiovascular mortality has made the most significant contributions to improvements in life expectancy for middle-aged and

older adults. Causes of death have become increasingly diverse in recent decades as a result of gains in life expectancy, with potential consequences for healthcare systems. The authors note that in specific periods, for both sexes, improvements in life expectancy were primarily due to reductions in mortality from digestive and respiratory diseases, as well as decreased mortality at very young ages (0 to 5 years). It is worth highlighting that recent studies in high-income countries have primarily focused on the effects of reductions in cardiovascular and cancer mortality on life expectancy improvements. While these causes are essential for directing public resource interventions, our aim here is to highlight distinctive features observed in the Italian context that are often overlooked in other studies.

More recently, global focus has shifted away from the primary causes of mortality, directing attention instead towards the phenomenon known as "Deaths of Despair" (Case & Deaton 2015). This category is perceived as a single class that encompasses a set of three distinct causes. The literature includes in the definition the mortality attributable to alcohol consumption, drug abuse, and suicide. These factors have been identified as contributing significantly to the increasing mortality rates among middle-aged individuals in the United States, where this phenomenon has been predominantly studied. Nevertheless, the mechanisms by which these trends potentially occur, behave, and evolve in other countries remain less well-known, and frequently neglected in research.

In this context, this study aims to examine the mortality trends of the deaths-of-despair causes, drug- and alcohol-related mortality, and suicide, in Italy, using a macroarea-level analysis. Specifically, we leverage a double lens of the potential gain in the life expectancy approach combined with the time series analysis to discover potential trends and impending changes in Death of Despair evolution.

In Section 2 we provide an overview of the topic Deaths of Despair: where it arose, in which countries it was addressed and what results were found. Section 3 contains information on the data and codes used to select the causes of death. Section 4 is devoted to explaining the methods used in the analyses. In Section 5 we set out the results we found with the national and Nuts1 analyses. Finally, Section 6 discusses the results and concludes the paper. Appendices A and B re-

spectively contain the distributions of Age-at-Death of despair and further results of the analyses at the Nuts1 level.

2 State of Art on Deaths of Despair

The term *Deaths of Despair* was coined by Case & Deaton (2015) and further explored in subsequent papers in 2017 and 2020. This term arises from the assumption, supported by evidence—at least in the United States—that deaths from these causes are associated to self-destructive behaviors reflecting a form of despair.

In their work, Case & Deaton highlighted an alarming increase in mortality rates among middle-aged non-Hispanic whites since the late 1990s, and in 2020, they described the ongoing crisis in the United States as an "Epidemic of Despair."

Outside the US, studies on trends in deaths of despair are limited but growing. For instance, Allik et al. (2020) reported that Scotland shows a similar trend to the US, particularly with a significant increase in drug-related deaths.

In other countries, the situation is less severe, A recent study by Dowd et al. (2023) compared the rest of the UK and Canada with the US and Scotland, and they did not observe such dramatic increases in deaths of despair. However, there has been an upward trend in drug-related deaths and suicides.

To broaden the discussion beyond English-speaking countries, some authors extended the analysis to other European and Southern European countries. King et al. (2022) compared the US with Eastern European countries, where they observed a similar health crisis linked to the rapid transition from socialism to capitalism. This transition led to an unprecedented increase in mortality, particularly among middle-aged men, due to economic dislocation, stress, and despair. Piñeiro et al. (2023) dealt with Deaths of Despair in Spain. The authors were particularly interested in the socio-economic aspects related to deaths of despair, highlighting significant educational inequalities, with lower educational attainment associated with higher mortality.

In this context, the present study aims to examine mortality trends related to deaths of despair—specifically drug- and alcohol-related mortality and suicide—in Italy, using a macroarea-level analysis. We adopt a dual approach, combining the potential gain in life expectancy with time series analysis, to identify potential trends and impending changes in the evolution of Deaths of Despair.

3 Data

We analyse trends in despair-related mortality in Italy across four decades from 1983 to 2018. The data on deaths and mid-year population estimates come from the Italian National Statistical Institute (ISTAT).

Data are provided at a provincial level; however, for this study, we decided to aggregate it to the NUTS1 level to gain a more comprehensive perspective on the phenomenon and to enhance the robustness of our statistical analyses. NUTS1 represents the major Italian group of regions: North-West (Valle d'Aosta, Lombardia, Piemonte e Liguria), North-East (Veneto, Emilia-Romagna, Friuli Venezia-Giulia and the Autonomous provinces of Bolzano and Trento), Centre (Toscana, Umbria, Marche and Lazio), South (Abruzzo, Campania, Molise, Puglia and Basilicata), and Islands (Sicilia e Sardegna).

The data is grouped into five-year age bands, up to 90+, and all analyses were conducted separately for males and females.

ISTAT data provide information on the leading cause of death, classified according to the ICD-9 system from 1983 to 2002, and the ICD-10 system from 2003 to 2018. For our analysis, we focused on the three specific causes of death associated with despair as highlighted in the literature (Alcohol and Drugs related mortality and Suicides). To select the deaths due to these causes we adopt the codes used by Piñeiro et al. (2023). In particular, we identified deaths related to alcohol as those coded under chronic liver disease and cirrhosis, including alcohol poisoning and other alcohol-related disorders. Drug-related deaths encompass mental and behavioral disorders due to drug use as well as accidental poisoning from drug exposure. Lastly, suicide deaths also

include cases where the intent is undetermined, acknowledging the challenges in accurately coding such sensitive cases. The corresponding ICD codes for these categories are detailed in Table 1. We caught some slight trend breaks in the transition between ICD9 and ICD10. However slight they are, the presence of trend breaks will be taken into consideration during the analysis of the time series.

	ICD-9	**ICD-10**
Alcohol	291, 303, 305.0, 357.5, 425.5, 535.3, 571 (excluding 571.6), E860	F10, K70, K73, X45, G31.2, G62.1, I42.6, K29.2, K74.0, K74.2, K74.6, K86.0
Drugs	292, 304, 305.2-305.9, E850-E858	F11-F16, F18-F19, X40-X44
Suicide	E950-E959, E980-E989	X60-X84, Y10-Y34, Y87.0, Y87.2

Table 1: Codes of Deaths of Despair as in Table 1 of Piñeiro et al. (2023).

4 Methods

4.1 Potential Gain in Life Expectancy

The *Potential Gain in Life Expectancy* (PGLE) is a theoretical measure that estimates the increase in life expectancy at birth if a specific cause of death were eliminated from a population (Tsai et al. 1978). This measure provides valuable insights into the relative impact of different causes of mortality on overall population health. In this framework, all the individuals in the population are assumed to be subject to a number of independent competing causes of death acting simultaneously (Lai et al. 1997). It is necessary to assume the causes of death as independent.

The number of years gained in life expectancy at birth is calculated by subtracting the usual life expectancy in the presence of all causes of death from that in the corresponding scenario in which one or all the causes of death under study are removed.

Then, defining D_x the death count at age x due to all causes of death, and $D_x^* = D_x - D_x^C$ the deaths due to all causes of death except the deaths due to the removed causes (D_x^C) we can compute two different mortality rates for each specific age (m_x and m_x^*), leveraging the same

mid-year exposure population (E_x). Consequently, two life tables are calculated based on the two mortality rates, each providing a life expectancy at birth: respectively, e_0 from all causes of death-life table and e_0^* from the life tables with cause elimination.

The potential gain in life expectancy is defined as:

$$PGLE = e_0^* - e_o \tag{1}$$

The Potential Gain in Life Expectancy is, therefore, a quantity measured in years that takes values between 0, if no death is due to one of the removed causes, to e_0, if all causes of death are removed.

The PGLE by construction takes into account the difference between the distribution of the age at death of the removed cause and that of all causes together. Removing deaths occurring at younger ages has a greater impact on life expectancy.

4.2 Cointegration Analysis

Cointegration Analysis is a tool useful to understand and model the dependence between time series variables (Arnold & Glushko 2022). We are interested in better understanding whether the impacts of despair-related causes of death within and between different parts of Italy are co-integrated, and so if there exist long-run equilibrium relationships between them.

We define, for example, a multivariate time series containing the impacts of a single cause of death in different areas for the same years. As defined by Engle & Granger (1987), the components of a multivariate time series are said to be cointegrated if they have an integration order equal to or higher than 1, and it is possible to arrange at least one linear combination out of them whose integration order is smaller than input series. This means that if the components are integrated of order 1, then they are cointegrated if there is at least one linear combination of them that is stationary (Cefalo et al. 2023).

Cointegration analysis has been developed in the field of econometrics, but has recently also

gained attention in longevity studies (De Santis & Salinari 2023) and mortality modelling (e.g. see Aburto et al. (2020), Nigri et al. (2022*a*)) and forecasting (Cardillo et al. 2023). Extensive use of cointegration analysis to study dependency links and the long-term equilibrium between causes of death using VECM models was made by Arnold & Glushko in several works (Arnold & Sherris (2013, 2015), Arnold & Glushko (2021, 2022)). We use a workflow similar to that used in these papers.

Let's define the multivariate time-series $\boldsymbol{y_t}$ that consists of the n Non-Stationary elements y_{it}, for $i, \ldots, n$ are said to be cointegrated with a cointegrating vector β if a linear combination $\beta' \boldsymbol{y_t}$ is stationary:

$$\beta_1 y_{1t} + \beta_2 y_{2t} + \cdots + \beta_n y_{nt} = z_t,$$

where z_t is a stationary variable of stochastic deviations.

To model Non-Stationary, but cointegrating time-series, VECM models were specified:

$$\boldsymbol{\Delta y_t} = \boldsymbol{c} + \boldsymbol{d}t + \boldsymbol{\Gamma_1 \Delta y_{t-1}} + \boldsymbol{\Gamma_2 \Delta y_{t-2}} + \cdots + \boldsymbol{\Gamma_{p-1} \Delta y_{t-p+1}} + \boldsymbol{\Pi y_{t-1}} + \boldsymbol{\epsilon_t},$$

Where $\boldsymbol{\Delta y_t} = \boldsymbol{y_t} - \boldsymbol{y_{t-1}}$ denote the first differences of the data time series, $\boldsymbol{c}$ and $\boldsymbol{d}$ are $n \times 1$ vectors of constants, $\boldsymbol{\Gamma_i}$ is a $n \times n$ matrix of autoregressive coefficients for $i, \ldots, p-1$, and $\boldsymbol{\epsilon_t}$ is the white noise term of the model. We are interested in $\boldsymbol{\Pi y_{t-1}}$, which represents the cointegrated term and provides the information on the long-run equilibrium between the time series: the rank of the matrix $\boldsymbol{\Pi}$ corresponds to the number of cointegration relations. Thus, if the rank of PI - henceforth, r - is greater than zero, the process is considered cointegrated. With $r = 0$, on the other hand, the processes $\boldsymbol{y_t}$ are devoid of cointegrating relationships. Johansen (1988) proposed two tests to identify the number cointegration relations, if they exist, via the trace and the maximum eigenvalues tests on matrix $\boldsymbol{\Pi}$.

We then define the steps to follow in order to define whether multivariate time series are cointegrated: first of all, we check that the time series that make up the multivariate time series are Non-Stationary and therefore present a unit root. We test the hypothesis of the presence of a unit root in the time series with the best-recognised tests: Augmented Dickey-Fuller (ADF) and

Phillips-Perron (PP). We also use the complementary Kwiatkowski-Phillips-Schmidt-Shin (KPSS) test in which the null hypothesis is the stationarity of the series. Analogously, but with opposite acceptance regions, we study the stationarity of the time series of first-order differences.

We then apply the Johansen approach to define whether cointegration links between the series are present and in what number. Finally, we test the stationarity of these relationships to ensure that they constitute a long-run dependency structure. All tests performed with critical values of 95%, unless otherwise reported.

5 Results

5.1 Decreasing impact of Deaths of Despair

To assess the impact of Deaths of Despair on the overall population health, we use the Potential Gains in Life Expectancy as explained in Section 4. Using the PGLE allows us to take into account the distribution of age at death of the causes considered. Suicide, Alcohol and Drugs have a different age-at-death distribution from all-cause mortality see Figure 3 in Appendix A. Removing deaths occurring at younger ages has a greater impact on the gain in life expectancy.

In Italy, the impact of deaths of despair on the population's overall health fell substantially between 1983 and 2018 see Figure 1. The PGLE value has more than halved over the period considered: the highest value calculated was in 1984 among men with almost a year of life lost ($\mathrm{PGLE} = 0.85\mathrm{y}$) due to all DoD, while the lowest is in 2018 when we calculated 0.4 years of life expectancy gained. For women, the gain in life expectancy went from 0.4 years in 1984 to 0.16 in 2018.

This decline is driven by alcohol-related mortality: the PGLE by removing this cause alone fell from 0.63y to 0.16y for men (from 0.31y to 0.07y for women). The impact of suicides and drug-related deaths has remained almost constant over time, leading to a convergence between these three causes of death.

As a consequence of the economic crisis of 2008, in the male population suicides exceeded

the impact of alcohol-related deaths in 2010, while among women only in the last year analyzed. In contrast to the evidence from the United States, where drug-related deaths have the highest impact, in Italy these have unremarkable levels compared to the others.

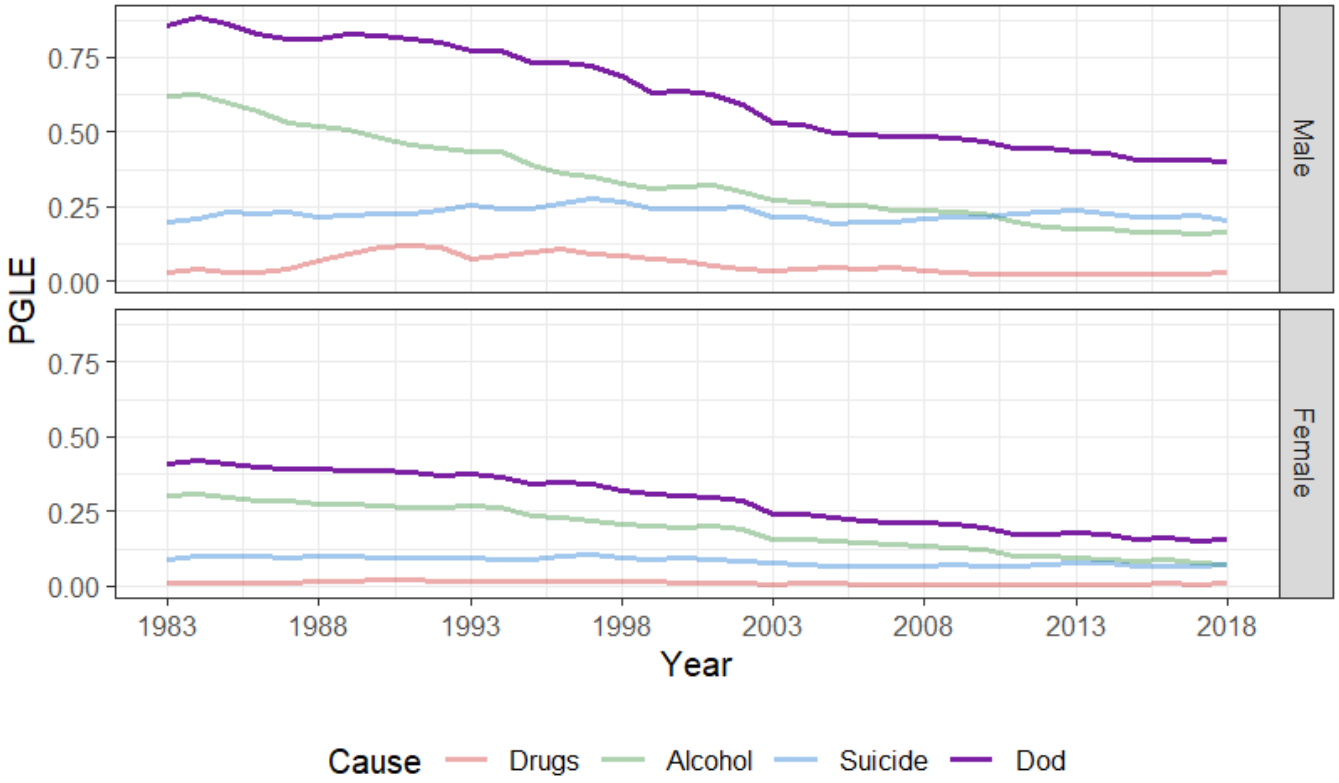

Figure 1: Potential Gain in Life Expectancy removing Drugs, Alcohol and Suicide separately or together (DoD, violet line). Italy 1983-2018.

In Italy, the North-South socio-economic gradient is well known (Istituto Nazionale di Statistica 2021, Moretti & Strozza 2022) and this is also reflected in inequalities in longevity and mortality (Istituto Nazionale di Statistica 2024, Federico et al. 2013) across the country, specifically for certain causes of death (Divino et al. 2009). We therefore believe that investigating the impact of deaths of despair at a more detailed level could provide a more comprehensive perspective on the phenomenon. In Figure 2 trends of PGLE for Italian macro-areas are reported.

Overall, we observe a similar trend in all macro-areas, but with some differences in the magnitude of the different causes of death. See also Figure 4 in Appendix B for a better understanding of the PGLE trend of the specific causes in the specific areas.

Considering the three aggregated causes (violet line) in the 1980s, the areas where the impact

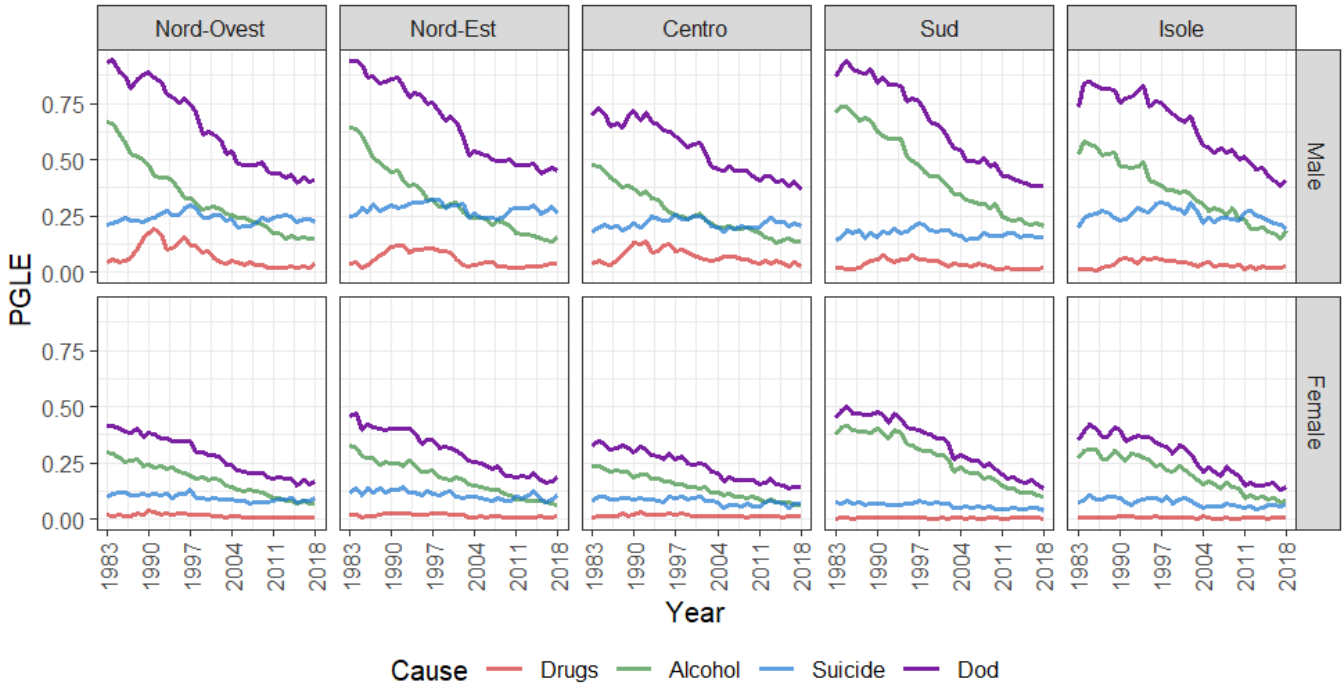

Figure 2: Potential Gain in Life Expectancy removing Drugs, Alcohol and Suicide separately or together (DoD, violet line). Nuts1 1983-2018.

of deaths of despair is greatest are the northern areas and the South, while in the Islands and especially in the Centre, the burden was less evident. In the last years analysed, we observe a process of convergence, but the North-East area continues to have the highest PGLE values.

More interesting observations arise from the analysis of the individual causes. Drug-related deaths are the least impacting, but we evidence high PGLE values mainly in the North and Centre during the 1990s (in 1990 for men in the North-West about 0.2 years of PGLE). In the last two decades, the impact of drug-related mortality has declined sharply, remaining higher in the Centre than in other areas.

In contrast, the Centre is the area that historically reports the lowest alcohol-related PGLE values. Concerning this cause, the highest values are observed, during the entire period, in the North (both East and West) and the South. Only in the latter area, however, the impact of alcohol-related mortality is still the highest of the three causes. In the North, Centre and Islands in the last years analysed, Suicide represents the most worrying cause of death (in 2018 for men in the North-East 3 months –0.25 years– of PGLE). The opposite trend between alcohol-related deaths

and suicides and the difference between the South and the other areas shows that the two causes are, at least in part, competitive. The reported findings are equally valid for both males and females, keeping in mind, however, that the values in the female population are much lower.

5.2 Cointegration analysis between and within areas

We observed very different trends between the three causes of the Deaths of Despair classification and also saw some differences and some similarities between the trends of the different areas concerning the individual causes. To identify whether a dependency structure exists in the Italian context between the causes that make up this new classification we use Cointegration Analysis as explained in the Section 4.2.

We are interested in finding out whether there is a long-run equilibrium between the three causes, which would indicate a common trend and thus a common reaction to "variations in despair" in Italy, and a long-run equilibrium between different areas of the country in the trend of each cause, which would indicate a homogeneous response of the country to "variations in despair".
We then indicate two types of analysis:

- **Within**-area: investigates the dependency structure of the three causes *within* each area,
- **Between**-areas: investigates the equilibrium of trends *between* each region concerning each cause.

We perform Cointegration Analysis on the time-series of PGLEs (showed in Figure 2) for each specific area and cause of death for both sexes (5 areas + all Italy, 3 causes + all of them together (DoD) and 2 sex = 48 time-series each with 35 years of observations). We then perform 4 within and 6 between analyses for each sex.

ADF, PP and KPPS tests report that 96.7% of the time series is Non-Stationary (all but PGLEs due to drugs in the Centre for males) with 0.05 p-value, and the 93.3% of the series are integrated of order 1.

Table 2 and Table 3 show all statistically significant relationships reported by Joahnsen's approach and whether the relationships found are stationary or not.

Table 2, contains the between-areas analysis results. A long-term equilibrium between PGLE trends obtained by removing all Deaths of Despair among women was revealed, and also by removing only drug-related deaths. A non-stationary relationship, so we cannot state that there is (a long-term) equilibrium, was shown between the trends in PGLE due to alcohol among males.

The within-area analysis (see Table 3) did not reveal any significant dependency structure among the causes of death from despair, even when the significance threshold was relaxed by increasing the p-value cutoffs from 0.05 to 0.1 or 0.25.

Table 2: Number of relation found with Joahnsen's eigen and trace test for each cause **between** Italian macro areas and whether these relationships are Stationary, meaning the evidence of a long-run equilibrium.

		Number of Relations	
DoD	Male	0	
	Female	1	Stationary
Sucide	Male	0	
	Female	0	
Alcohol	Male	1	Non-Stationary
	Female	0	
Drugs	Male	0	
	Female	2	Stationary

5.2.1 Short-run Equlibrium

As mentioned in the section, we note slight trend breaks in the transition from ICD9 to ICD10 classification for the different causes. We therefore propose the same within and between analyses on the two sub-periods 1983-2002 and 2003-2018.

Generally, the use of cointegration analysis is suggested on extended time series: the larger the sample, the more reliable the evidence. The results reported here are consequently less reliable than those on a long-term basis, but we believe they can help to get a clearer idea of the long-term dynamics. In both sub-periods, more than 90% of the time series are Non-Stationary (95.8% and 93.8% respectively) and the percentage of integrated series of order 1 decreases over the whole

Table 3: Number of relation found with Joahnsen's eigen and trace test **within** Italy and each Italian macro-areas between the three causes together and separately and whether these relationships are Stationary, meaning the evidence of a long-run equilibrium.

		Number of Relations
Italy	Male	0
	Female	0
North-West	Male	0
	Female	0
North-East	Male	0
	Female	0
Centre	Male	0
	Female	0
South	Male	0
	Female	0
Islands	Male	0
	Female	0

period (77.1% and 54.2%).

No short-run equilibrium is shown in the analysis within, confirming that the trend of the three causes at the national level and in the individual macro-areas is completely independent and unrelated. In contrast, we find some equilibrium relationships for individual causes within the macro-areas. The results are summarised in Table 4. Most of the cointegration relationships detected did not turn out to be statistically stationary, so we cannot identify a short- (or long-term) equilibrium in these relationships. On the other hand, the trend in alcohol-related PGLE in the female population between 1983 and 2018 is in equilibrium. Throughout the ICD10 classification, the time series of the drug- and alcohol-related PGLEs of men in the Nuts1 areas are in equilibrium.

The cointegration analysis on the sub-periods confirms the absence of a dependency structure between the 3 causes nationally and within each macro area. At the same time, there are stationary (and non-stationary) cointegration relations between the Nuts1 areas for some of the causes.

Table 4: For each multivariate time series is reported if there are **Stationary** cointegrating relationships, *Non-Stationary* relationships or there are *No Relations*. Bold values indicate stable equilibrium.

		1983-2002 (ICD9)	**2003-2018 (ICD10)**
DoD	Male	No relations	Non-Stationary
	Female	Non-Stationary	Non-Stationary
Suicide	Male	No relations	Non-Stationary
	Female	No relations	Non-Stationary
Alcohol	Male	Non-Stationary	**Stationary**
	Female	**Stationary**	Non-Stationary
Drugs	Male	No relations	**Stationary**
	Female	No relations	Non-Stationary

6 Discussion

We studied the "Deaths of Despair" trend in Italy, an example of a low-mortality country, in the pre-COVID-19 period (1983-2018). Deaths of despair are considered to be those related to alcohol and drug abuse and suicides. In the United States, Case & Deaton (2020) reported a real "Epidemic of Despair". Other countries showed a similar worrying trend, albeit with a lower mortality rate. In Italy, the problem of death of despair does not have the magnitude it has in other countries, especially in the US.

The study of Deaths of Despair with Italian data is new, so we first conducted an exploration of the phenomenon using the *Potential Gain in Life Expectancy* calculation. The PGLE provides a descriptive measure of the magnitude of the analyzed causes on the overall population health. It takes implicitly into account the number of deaths and the age-at-death distribution of the causes.

As the name implies, the literature considers these deaths to be related to forms of despair, thus moving in the same direction as despair in society. Therefore, we investigated whether there is a long-term balance in the mortality trend for the three causes in Italy. For this purpose, we leverage *Cointegration Analysis* of time series.

6.1 Main findings

We have found a decline in the impact of deaths due to the three causes considered on the population's overall health. The decline is driven by the decline in alcohol-related mortality. Moreover, we noticed some differences with the US in the magnitude of the three causes. In our analysis, alcohol has the highest magnitude for most years, leaving the lead to suicide in the years following the 2008 economic crisis. In contrast to the US, drug-related mortality consistently has the lowest magnitude.

Analyzing these causes as a single group in Italy may lead to biased and overly optimistic considerations. In spite of the decline overall, as we have said, the impact of Suicides has slightly increased or remained constant, as has that of drug-related deaths in some years (e.g., at the turn of the 1980s and 1990s). In addition, the trend is not homogeneous if we investigate this classification across the country.

We, therefore, wondered whether there is a dependency structure among these three causes in Italy, which would indicate a homogeneous response to variations in despair, or at least a homogeneous behaviour of the group as a whole. At the same time, we are interested in understanding whether there is a dependency structure (i.e. an equilibrium) in mortality trends among different areas of the country for each cause. To answer these two questions, we used the Cointegration Analysis. This technique identifies whether a long-term relationship exists between two or more non-stationary time series. The Cointegration Analysis provided evidence that was entirely opposite to the hypothesis of dependence between causes, both within the country and within each Nuts1 macro-areas. Only in two cases emerged a long-term equilibrium: between the trend in deaths of despair overall and for drug-related mortality for the female population across the country.

To ensure the robustness of our findings and to check whether a bias was present due to the change from ICD9 to ICD10, we performed the analyses on two sub-periods. Once again, the three causes are devoid of cointegrating relationships, whereas some relationship arose between the trends in the regions. This may suggest that, in certain sub-periods, the country addressed

some of the different causes evenly across its regions.

6.2 Conclusion

Our findings support the idea that in Italy these causes should be analysed separately and not aggregate the data as Deaths of Despair. Due to the lack of structural dependence and equilibrium in the trends of the three causes, we argue that they represent three distinct outcomes of despair. In Italy Drugs, Alcohol and Suicide strike at different ages and differently across regions (in most cases) to be treated as a single cause of death under the name Deaths of Despair.
At the same time, we believe monitoring and studying these causes of deaths is necessary. Although in Italy the problem is not as worrying as in the United States, in the last year of the analysis (2018) the life expectancy lost due to these causes is in total almost 5 months. Other studies dealing with Deaths of Despair in Italy, exploring the causes separately, can untangle their link with despair and identify which factors to address to continue the decline in their impact.

Hence, future studies on the Deaths of Despair in Italy should focus on grasping the links between socio-economic aspects and these causes to indicate how they are related to despair in Italy. For this purpose, it is important to study the phenomenon at a greater level of detail (such as the provincial level) and to include in the analyses the years of the Covid-19 pandemic, which in other countries had an impact on these causes of deaths Angus et al. (2023).

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A Age-at-Death of Despair Distribution

The age-at-death distribution varies between the three causes, between sexes and across time.

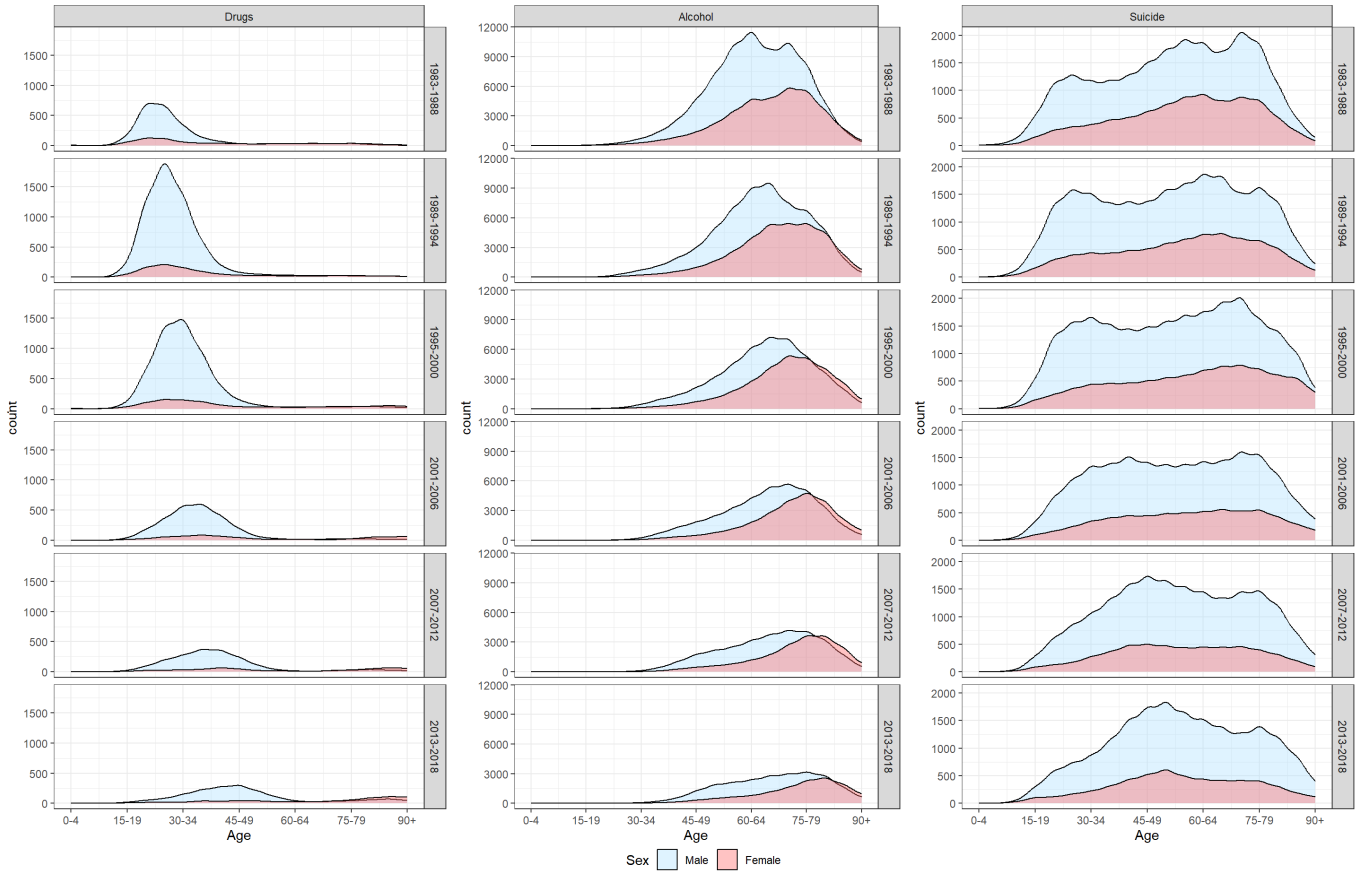

Figure 3: Distribution of age at death for each of the 3 causes within deaths of despair grouped in 5-year intervals. Italy 1983-2018.

Looking at Figure 3 we can see that the modal age-at-death related to drug abuse shifted on the left over time. For both males and females, there is a peak in the frequency of drug-related deaths in the 1990s. At higher ages there is an increase in the curve for females, we assume this is mainly due to deaths related to mental and behavioural disorders due to use of drugs and accidental poisoning due to poorly recorded medical treatment. In any case, the numbers are small and do not interfere with the analysis carried out.

Alcohol-related deaths also have a modal age moving towards older ages over the years, especially among men marking a convergence with the modal age at death from alcohol for women,

but maintaining higher variability.

Suicide has a bimodal distribution. The first of the two modes (the one around age 50) increased for males and females over time. Of the three causes, suicides have the greatest variability in the age-at-death.

B Potential Gain in Life Expectancy at Nuts1 level

The measure of Potential Life Expectancy Gain is a measure that can be compared between different regions, different years, different genders, and different causes of death. The measure of Potential Life Expectancy Gain is a measure that can be compared between different regions, different years, different genders and different causes of death. Figure 4 shows all the calculated values in a single scale, so that comparisons can be made concerning each dimension.

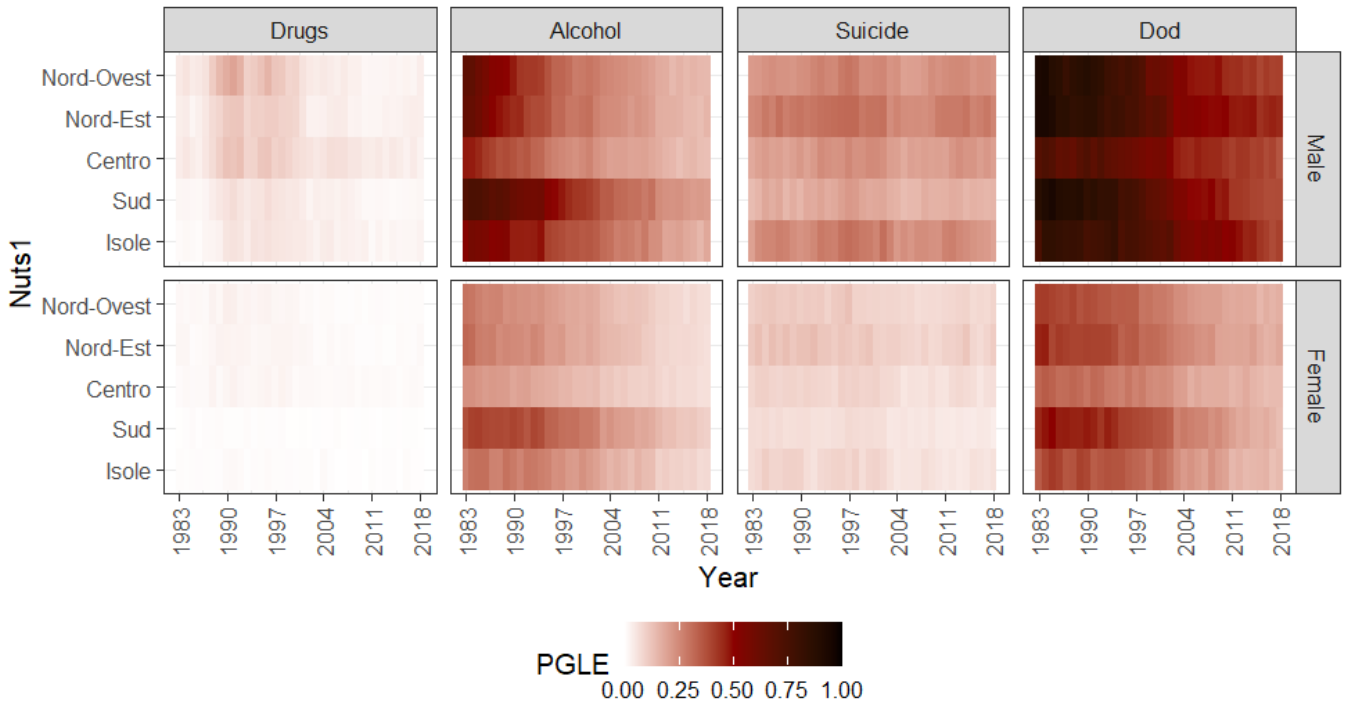

Figure 4: Heat Map of PGLE by causes of deaths separately or together. Darker colors represent higher Potential Gain value. Nuts1 1983-2018.

Most of the comments were reported in Section 5.2. Here we would like to highlight just a few additional aspects. The Centre reports the darkest colours in the drug-related PGLE, for both

males and females. The South stands out in alcohol-related mortality and the North-East and Islands in Suicide-related heat maps. The North-West maintains medium-high levels in each of the causes.