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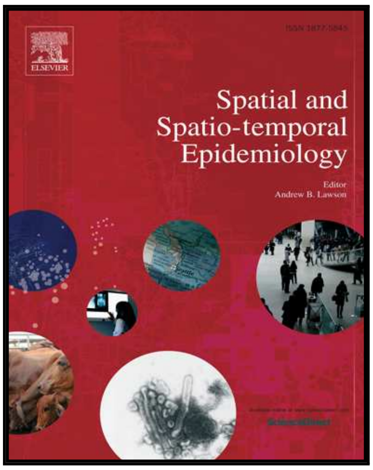
McNally, R, James, P, Blakey, K et al. (3 more authors) (2017) Can changes in population mixing and socio-economic deprivation in Cumbria, England explain changes in cancer incidence around Sellafield? Spatial and Spatio-temporal Epidemiology, 21. pp. 25-36. ISSN 1877-5845

https://doi.org/10.1016/j.sste.2017.02.002



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PII: S1877-5845(16)30027-2
DOI: 10.1016/j.sste.2017.02.002
Reference: SSTE 209

To appear in: *Spatial and Spatio-temporal Epidemiology*

Received date: 25 April 2016
Revised date: 14 February 2017
Accepted date: 21 February 2017

Please cite this article as: Richard J.Q. McNally , Peter W. James , Karen Blakey , Nermine O. Basta , Paul D. Norman , Mark S. Pearce , Can changes in population mixing and socio-economic deprivation in Cumbria, England explain changes in cancer incidence around Sellafield?, *Spatial and Spatio-temporal Epidemiology* (2017), doi: 10.1016/j.sste.2017.02.002

Can changes in population mixing and socio-economic deprivation in Cumbria, England explain changes in cancer incidence around Sellafield?

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Abstract

Previously excesses in incident cases of leukaemia and non-Hodgkin lymphoma have been observed amongst young people born or resident in Seascale, Cumbria. These excesses have not been seen more recently. It is postulated that the former apparent increased risk was related to ‘unusual population mixing’, which is not present in recent years. This study investigated changes in measures of population mixing from 1951-2001. Comparisons were made between three specified areas. Area-based measures were calculated (migration, commuting, deprivation, population density). All areas have become more affluent, although Seascale was consistently the most affluent. Seascale has become less densely populated, with less migration into the ward and less diversity with respect to migrants’ origin. There have been marked changes in patterns of population mixing throughout Cumbria. Lesser population mixing has been observed in Seascale in recent decades. Changes in pattern and nature of population mixing may explain the lack of recent excesses.

Key words: Deprivation; England; Leukaemia; Population Mixing; Socio-economic

1. Introduction

An excess rate of acute lymphoblastic leukaemia and non-Hodgkin lymphoma has been found in children and young people resident in Seascale, Cumbria, UK during 1963-1990 which has been discussed in relation to Sellafield, a nuclear fuel reprocessing and decommissioning site (Draper et al., 1993). However, this apparent cluster was not observed when more recent data, including cases diagnosed during the period 1991 to 2006, were analysed (Bunch et al., 2014).

Kinlen suggested that excesses in incidence of childhood leukaemia would be observed in those locations that experienced an ‘unusual’ type of population mixing, with high levels of migration into a previously isolated area (Kinlen, 1988; Kinlen, 1995). Kinlen based his hypothesis on the findings of a number of studies from the UK which specifically related to areas of ‘unusual’ rural population mixing. These included areas with a high proportion of residents in the least deprived social class, areas with the highest ratios of wartime evacuee children compared with local children, areas with the largest proportion of oil workers, rural new towns with a greater density of children and greater diversity of origin than overspill towns and in areas that had the highest proportions of servicemen (reviewed by Little, 1999). Five studies from Croatia, France and the UK (including war situations and urban areas) found significant excesses in incidence associated with general higher levels of population mixing (Stiller and Boyle, 1996; Dickinson and Parker, 1999; Boutou et al., 2002; Dickinson et al., 2002; Labar et al., 2004). In contrast, two studies from the UK found deficits in incidence associated with increased population mixing (Parslow et al., 2002; Law et al., 2003). A Canadian study found a significant excess in incidence for rural areas where population growth had exceeded 20% (Koushik et al., 2001). Another study, from Hong Kong, found spatial clustering of incident cases in areas of extreme population mixing (Alexander et al., 1997).

In spite of the plethora of studies that have considered the putative link between population mixing and increased risk of childhood cancer (especially leukaemia) there has been no general consistency in the definitions used for ‘population mixing’ (Law et al., 2008). To address this, Taylor and colleagues compared a number of different measures of population mixing which were derived from UK census data. Hospital admissions data on infections were used as a proxy for level of community infections. The analyses found that commuting distance was a consistent measure of population mixing, as related to infectious disease and that both deprivation and population density were good proxies for infectious exposure. The investigators also noted that areas with high levels of population mixing do not necessarily have high rates of hospital admissions for infectious disease (Taylor et al., 2008). It is important to note that infectious exposures are particularly relevant to the hypotheses concerning the origin of childhood leukaemia (McNally and Eden, 2004).

We sought to determine if the dissipation of the cluster in Seascale could be explained by changes over time in the patterns and nature of population mixing. Given the availability of small-area population density over a prolonged time span, we have analysed the temporal changes in key measures of population mixing in relation to ‘Seascale’ and the surrounding areas (‘Allerdale plus Copeland without Seascale’ and ‘Cumbria without Seascale’). This report considers the period from 1951 to 2001 as a context for the previous analyses for 1963-1990 (Draper et al., 1993) and 1991-2006 (Bunch et al., 2014).

The aims of the study were to investigate patterns and temporal changes in different measures of population mixing in Cumbria and the following three specific geographical areas: (i) ‘Seascale’, (ii) ‘Allerdale plus Copeland without Seascale’, and (iii)

'Cumbria without Seascale'. Note that Seascale lies within Copeland district, and that Copeland and the adjacent district of Allerdale both lie within the county of Cumbria (Figure 1).

2. Materials and methods

The following measures of population mixing were used: *migration*, *commuting*, *deprivation* and *population density* (Taylor et al., 2008).

Migration was defined as a person moving their residential address into a ward (a census small area) in the study areas within one year of the census (this will largely be sub-national migration rather than immigration). Three separate types of migration-based population mixing were calculated for each ward as follows:

- Diversity – the Shannon index (Shannon, 1948), measuring the diversity of origins of in-migrants to the ward;
- Volume – $\log_e$ (proportion of in-migrants within the ward);
- Distance – $\log_e$ (median distance moved by in-migrants to the ward).

To investigate both local and more distant migration, these measures were calculated for distances above a threshold which varied from 0 to 300 km.

Commuting was defined as the daily and/or regular movement of an individual from home to a work place outside their residential ward. Three separate types of commuting-based population mixing were calculated for each ward as follows:

- Diversity – Shannon index (Shannon, 1948), measuring the diversity of origins of commuters into each ward;
- Volume – $\log_e$ (proportion of commuters into each ward);
- Distance – $\log_e$ (median distance commuted by commuters into the ward).

Each of these measures of commuting was calculated for those aged '16-59 years' only. Again, to investigate both local and more distant migration, these measures were calculated for distances above a threshold which varied from 0 to 100 km. It should be noted that for 1991 commuting measures at ward level were only available as a ten percent sample of the population and subject to data blurring and so this precluded calculation of these measures for Seascale for that census year.

Deprivation was measured using the Townsend index (Townsend et al., 1988). This is a composite socio-economic index which is derived from the standardized census based area proportions of unemployment, household overcrowding, car non-ownership and housing non-owner occupiers. The four separate components of the Townsend index were also analysed.

Population Density was defined as persons per km^2 within each geographical area. It was calculated for 'all ages', for ages '0-14 years', '15-24 years' & '0-24 years'.

There were six decennial censuses between 1951 and 2001. All measures were available for the 1981, 1991 and the 2001 censuses. In addition deprivation data were available for the 1971 census and population density was available for all censuses from 1951 to 2001. For both *migration* and *commuting*, and for the two areas comprising multiple wards (i.e. 'Cumbria without Seascale' and 'Allerdale plus Copeland without Seascale'), mean values are reported for *diversity* and *volume* and medians for *distance* measures.

3. Results

3.1. *Migration* (Figure 2, Figure 3, Figure 4)

There was greatest *diversity* of origin of migrants moving into Seascale in 1981 and least *diversity* in 1991. For wards in the area comprising 'Allerdale plus Copeland without Seascale' no pattern in mean *diversity* was seen. For wards in the area comprising 'Cumbria without Seascale' there was a small increasing trend in mean *diversity* from 1981 to 2001.

There was greatest *volume* of migration into Seascale in 1981 and least volume in 1991. For wards in the area comprising ‘Allerdale plus Copeland without Seascale’, the mean *volume* of migration was greatest in 2001, but there was little difference between 1981 and 1991. For wards in the area comprising ‘Cumbria without Seascale’, there was a small increasing trend in the mean *volume* of migration from 1981 to 2001.

The *distance* measure showed that no consistent patterns were observed in any of the three areas: Seascale, ‘Allerdale plus Copeland without Seascale’ and ‘Cumbria without Seascale’.

3.2. Commuting (Figure 5, Figure 6, Figure 7)

The *diversity* measure showed that for Seascale no change was observed from 1981 to 2001. For wards in the areas comprising ‘Allerdale plus Copeland without Seascale’ and ‘Cumbria without Seascale’, no consistent patterns were observed in mean *diversity* of commuting.

The *volume* measure showed that for Seascale no change was observed from 1981 to 2001. For wards in the areas comprising ‘Allerdale plus Copeland without Seascale’ and ‘Cumbria without Seascale’, no consistent patterns were seen in mean *volume* of commuting.

The *distance* measure showed that for Seascale there was generally greater distances commuted in 1981 compared with 2001. For wards in the area comprising ‘Allerdale plus Copeland without Seascale’ no consistent pattern was observed. For wards in the area comprising ‘Cumbria without Seascale’ median commuting distances were generally greatest in 1981.

3.3. Deprivation (Table 1)

Analysis of the overall *Townsend score* showed that, for all three areas, there was a trend towards decreasing deprivation between 1971 and 2001. Seascale has consistently remained the most affluent area.

Analysis of *area-level unemployment* showed no trends for all three areas. However, the lowest levels of unemployment were seen in Seascale, followed by 'Cumbria without Seascale', with the highest levels in 'Allerdale plus Copeland without Seascale'.

Analysis of *area-level household overcrowding* showed that, for all three areas, there was a trend towards decreased levels of household overcrowding between 1971 and 2001. The lowest levels of household overcrowding were consistently seen in Seascale.

Analysis of *area-level non-car ownership* showed that, for all three areas, there was a trend towards higher levels of car ownership. The highest levels of car ownership, much higher than other areas, were consistently seen in Seascale.

Analysis of *area-level non-home ownership* showed that, for all three areas, there was a trend towards higher levels of home ownership. Seascale only achieved the highest levels of home ownership in 1991 and 2001 compared with the other areas.

3.4. Population density (Table 2)

For 'all ages', Seascale had markedly lower levels of population density than other areas for all censuses (1951, 1961,…..,2001). 'Allerdale plus Copeland without Seascale' had the highest levels of population density for all censuses. For ages '0-14 years', '15-24 years' and '0-24 years', Seascale consistently had the lowest population density, followed by 'Cumbria without Seascale' and then 'Allerdale plus Copeland without Seascale'. For all three areas, there was a trend towards lower population density through time, especially for young people.

4. Discussion

The following key findings were made: (i) Seascale has become less densely populated; (ii) there has been less migration into Seascale; (iii) Seascale has become less diverse with respect to the origin of migrants; (iv) Seascale was the most affluent area and this was consistent across censuses; and (v) all areas have become more affluent. There was evidence of clustering of childhood leukaemia (ages 0-14 years) in Seascale for cases diagnosed during 1963-1983, but not during 1984-1990, nor 1991-2006 (Bunch et al., 2014). It is interesting to note that deprivation changed markedly in all areas between the 1981 and 1991 censuses. However, population density based on all ages, was lower in 1991 compared with 1981 for Seascale, but remained static in the other areas. Also, for Seascale, but not the other areas, there was a marked change in the diversity of origin of migrants moving into Seascale and in the volume of migration into Seascale between 1981 and 1991.

Kinlen's studies all relate to situations and locations where there have been a rapid change in populations due to wartime evacuation or socio-economic development, including that related to the building of new towns, the oil industry and the nuclear facility adjacent to Seascale village (Kinlen, 1988; Kinlen, 1995; Little, 1999). An alternative, but related hypothesis has been proposed by Greaves (Greaves, 1988). He suggested that precursor B-cell acute lymphoblastic leukaemia arises from at least two separate mutations. The first mutation occurs in utero, or around the time of birth creating a pre-leukaemia cellular clone. The second (or final) mutation occurs later and leads to the onset of leukaemia. Greaves indicated that infections would promote the second (or final) mutation. Delays in the usual exposure of the immune system to infection could increase the number of potentially susceptible pre-leukaemia cells and so increase the probability of the occurrence of the second (or final) mutation. Social and geographical isolation could lead to such situations where susceptible children may have had delays in exposure to infections (McNally and Eden, 2004). If delays in exposure to infection have become much more geographically widespread than in previous decades then it might be predicted that geographical clusters, such as the cluster at Seascale, would no longer be observed.

A previous study of childhood leukaemia in Cumbria analysed a birth cohort and used individual and community-level data to determine measures of population mixing (Dickinson and Parker, 1999). That study found that population mixing was a statistically significant risk factor for acute lymphoblastic leukaemia and non-Hodgkin lymphoma, particularly in young children. However, it is important to note that the study considered a cohort of children born from 1969-1989 to mothers resident in Cumbria, which includes the period when the Seascale cluster occurred. As similar data on births in Cumbria are not available for those born from 1990 onwards, it is not possible to repeat the same analyses for the most recent time period.

A national (England and Wales) study of population mixing and childhood leukaemia and non-Hodgkin lymphoma found increased risk of childhood leukaemia associated with greater levels of inward migration, especially from outside the geographical region. However, this was significant only for urban locations, but also with some evidence apparent for affluent rural areas (Dickinson et al., 2002). Another national study from England and Wales of childhood leukaemia found increased risk associated with diversity of incomers, particularly in rural areas (Stiller et al., 2008). However, a population-based case-control study from Finland did not find any association between residential mobility and increased risk of childhood leukaemia (Järvelä et al., 2016). Furthermore a census-based cohort study from Switzerland found no association between risk of childhood leukaemia and population growth, in-migration and diversity of origin (Lupatsch et al., 2015). Kinlen has suggested that inconsistency between studies may be due to differences in the definition of population mixing (Kinlen, 2012).

Our analyses have shown that there have been differences in the changes for volume and diversity of migration between Seascale and the other parts of Cumbria (‘Allerdale plus Copeland without Seascale’ and ‘Cumbria without Seascale’). For Seascale, there was a decrease in the level of population mixing. However, in general, in the other parts of Cumbria there was an increase in the levels of population mixing. It would be predicted that greater levels of population mixing throughout the other parts of Cumbria (and indeed throughout the whole of England) would lead to less opportunity for situations such as Seascale to arise (i.e. a very isolated area which experienced a rapid population influx when a large high-tech facility offered new employment opportunities).

The methods used in the present study to analyse population mixing had previously been evaluated by Taylor and colleagues (Taylor et al., 2008). However, it should be noted that they tested the measures using data on hospital admissions for infections. Such data on hospital admissions may not be reliably recorded and may not truly reflect the underlying burden of infections in the associated residential areas due to most infections not resulting in hospital admission.

In conclusion, there have been marked changes in the patterns of population mixing in Cumbria. It is especially noteworthy that Seascale has become less densely populated in recent decades with less migration into the ward and less diversity with respect to the origin of migrants. Changes in the pattern and nature of population mixing may explain the lack of recent excesses in incidence of cancer in children and young people born or resident near Seascale (Bunch et al., 2014). Further research should include investigating such changes in measures of population mixing in other areas where excesses have been reported and should also consider different measures of population mixing and rate of change in such measures.

Acknowledgements

This report is independent research commissioned and funded by the Department of Health Policy Research Programme ('Changes in Population Mixing and Socio-Economic in Cumbria', PR-ST-1214-00012). The views expressed in this publication are those of the author(s) and not necessarily those of the Department of Health.

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Table 1 Deprivation summary.

Area [a,b]	1971	1981	Census Year 1991	2001
Townsend Deprivation Score				
1. Seascale	-1.19	-1.64	-3.95	-4.25
2. Allerdale plus Copeland without Seascale	2.89	2.38	-0.03	-2.05
3. Cumbria without Seascale	1.69	1.37	-0.83	-2.70
Unemployment %				
1. Seascale	2.36	3.96	3.53	3.10
2. Allerdale plus Copeland without Seascale	4.78	10.42	8.98	4.41
3. Cumbria without Seascale	3.49	8.56	6.95	3.45
Overcrowding %				
1. Seascale	1.64	0.94	0.46	0.49
2. Allerdale plus Copeland without Seascale	6.32	3.17	1.29	0.76
3. Cumbria without Seascale	5.46	2.73	1.25	0.78
No Cars %				
1. Seascale	19.51	15.83	12.12	10.06
2. Allerdale plus Copeland without Seascale	48.82	38.87	32.43	25.61
3. Cumbria without Seascale	45.92	36.75	30.58	24.06
Home not owned %				
1. Seascale	56.64	47.74	18.94	18.56
2. Allerdale plus Copeland without Seascale	55.86	50.16	34.50	31.00
3. Cumbria without Seascale	49.27	43.05	30.18	27.40

Footnotes:

(a) Deprivation for areas 2 and 3 are calculated from Townsend ward data (Norman, 2010) with all age ward population as weights.

(b) Seascale is excluded from Copeland & Allerdale and from Cumbria.

Table 2. Population density summary.

Area [a,b,c]	1951	1961	Census Year 1971	1981	1991	2001
All ages						
1. Seascale	20.8	27.6	25.8	22.9	20.7	20.5
2. Allerdale plus Copeland without Seascale	86.5	89.0	88.1	90.9	90.5	87.9
3. Cumbria without Seascale	64.3	65.0	66.0	67.9	68.6	68.8
Age 0-14						
1. Seascale	5.0	7.1	6.2	4.2	3.4	3.4
2. Allerdale plus Copeland without Seascale	20.7	22.6	21.6	18.7	17.1	15.7
3. Cumbria without Seascale	14.5	15.4	15.6	13.5	12.4	12.1
Age 15-24						
1. Seascale	2.6	4.0	3.8	3.9	2.4	1.5
2. Allerdale plus Copeland without Seascale	11.9	11.7	12.8	14.0	11.9	9.3
3. Cumbria without Seascale	8.5	8.3	9.2	10.2	9.0	7.2
Age 0-24						
1. Seascale	7.7	11.1	10.0	8.1	5.7	4.9
2. Allerdale plus Copeland without Seascale	32.6	34.2	34.3	32.7	29.0	25.0
3. Cumbria without Seascale	23.1	23.7	24.7	23.7	21.5	19.3

Footnotes:

(a) Density is persons per square km.

(b) Seascale is excluded from Copeland & Allerdale and from Cumbria

(c) Population figures for Copeland & Allerdale and Seascale for years 1951, 1961 and 1971 estimated as for 2001 census boundaries using geoconversion methods (Norman et al., 2003) and population estimates of past populations (Rees et al., 2004).

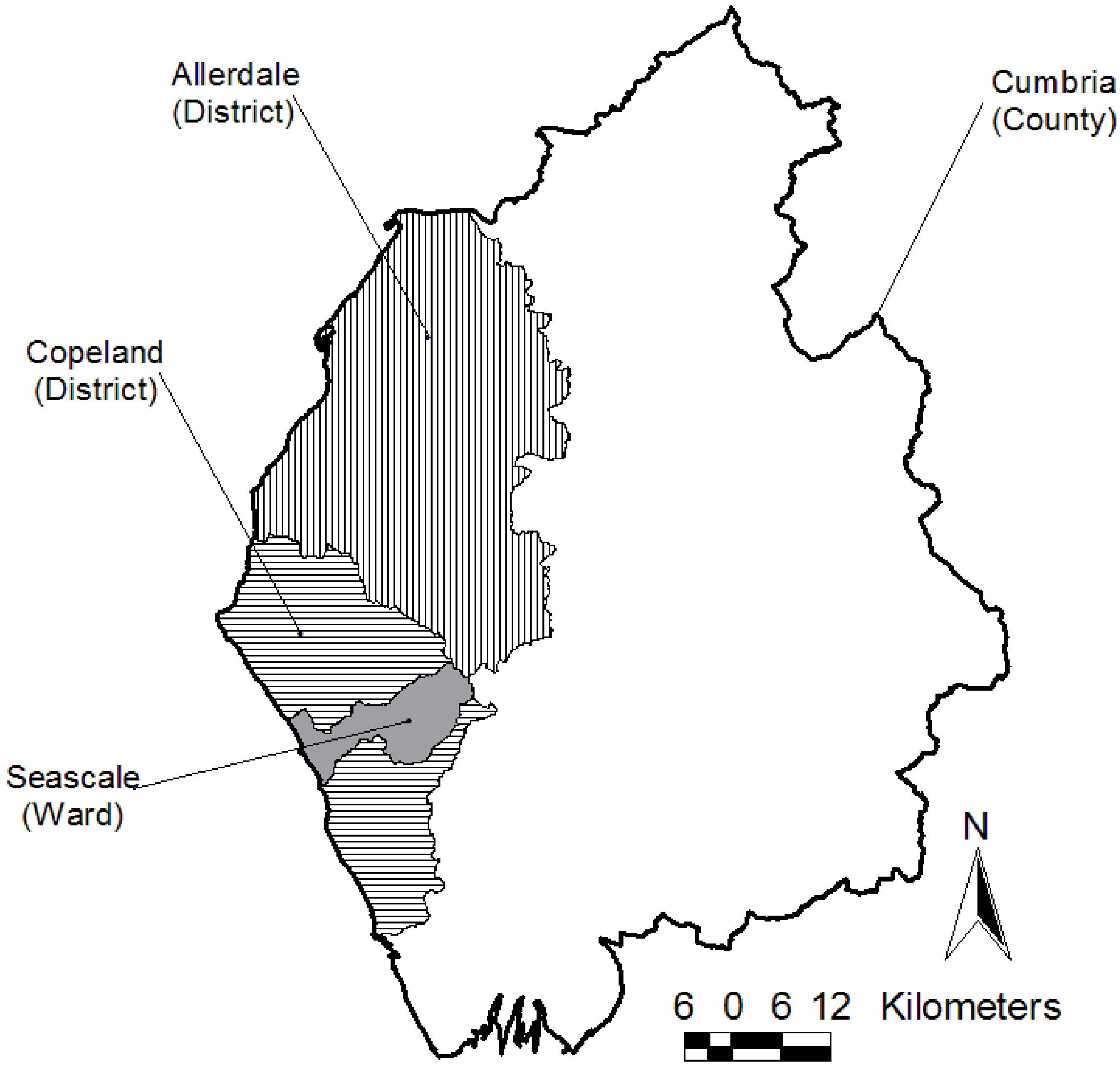


Figure 1. Geographical relationships of Seascale ward with Copeland and Allerdale districts and Cumbria county.

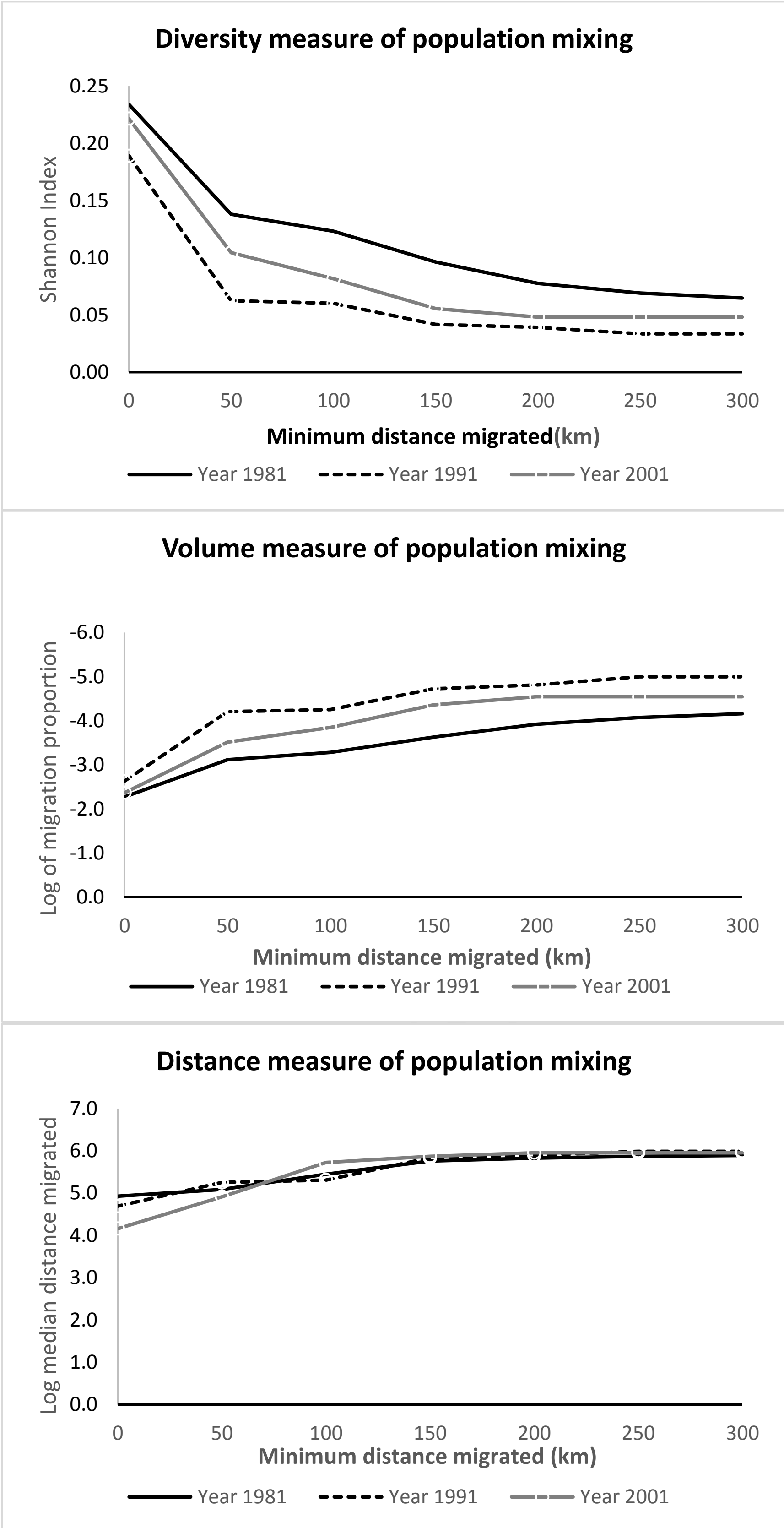


Figure 2. Population mixing due to migration: Seascale.

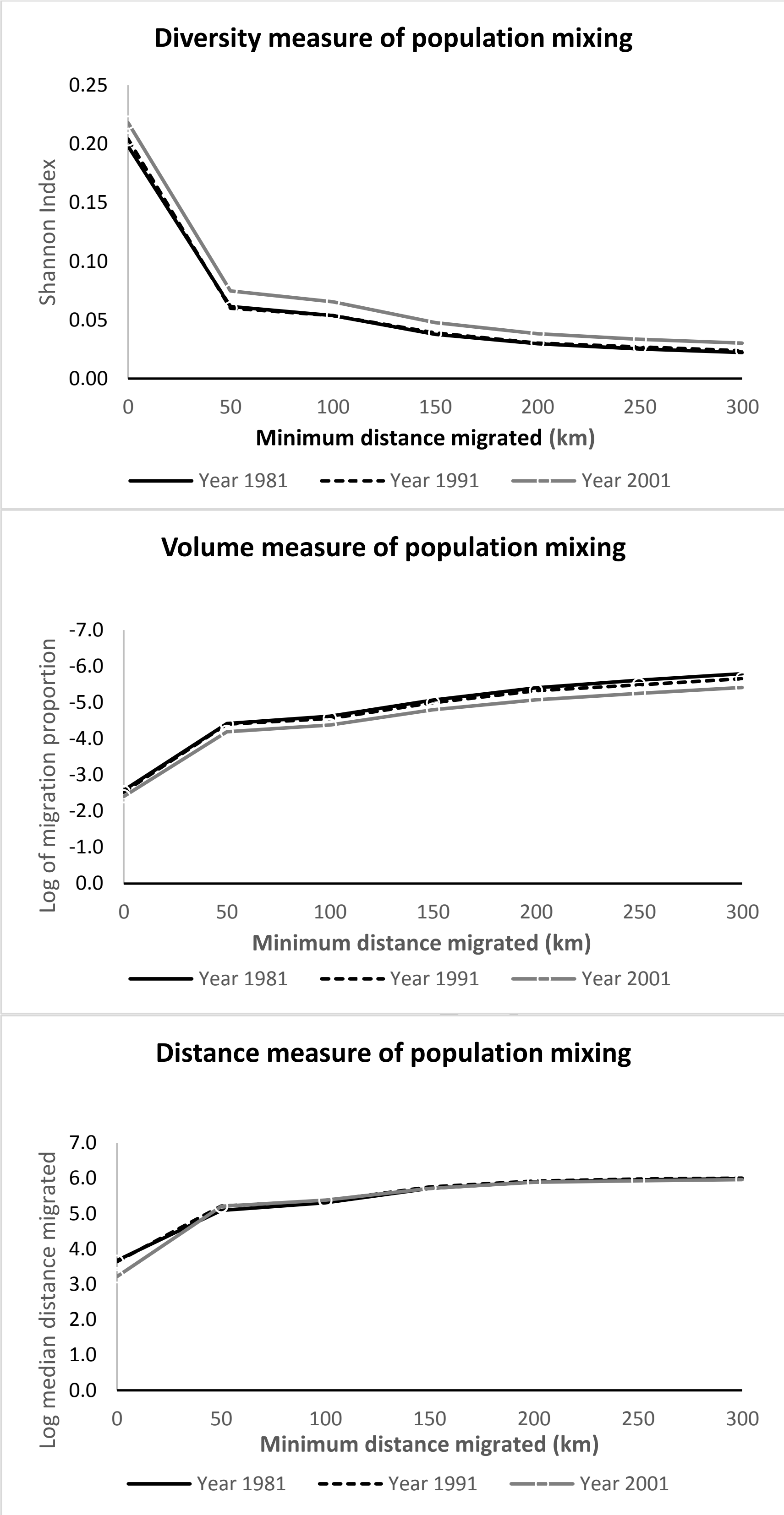


Figure 3. Population mixing due to migration: Allerdale plus Copeland without Seascale Mean value reported for diversity and volume and median for distance measure.

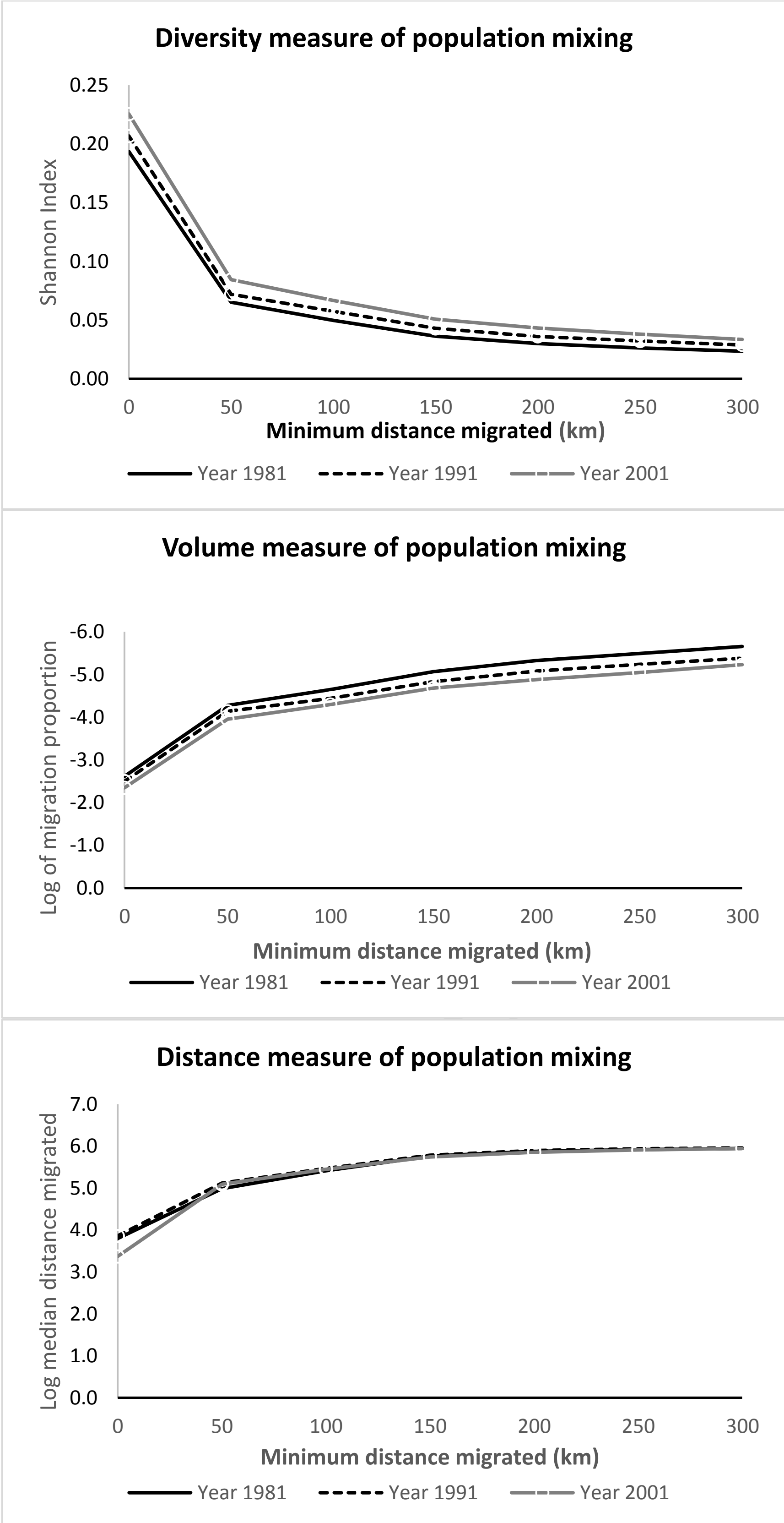


Figure 4. Population mixing due to migration: Cumbria without Seascale.Mean value reported for diversity and volume and median for distance measure.

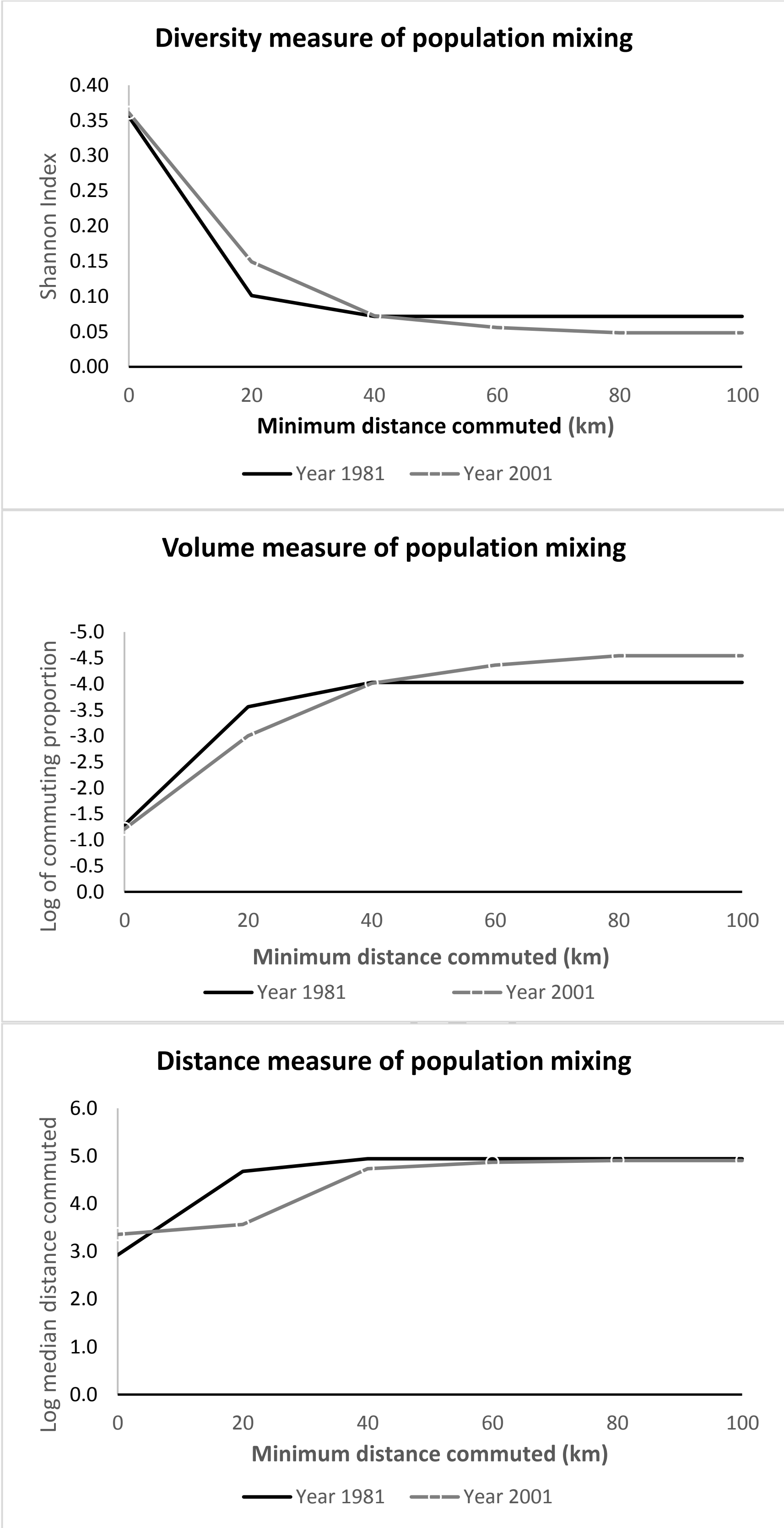
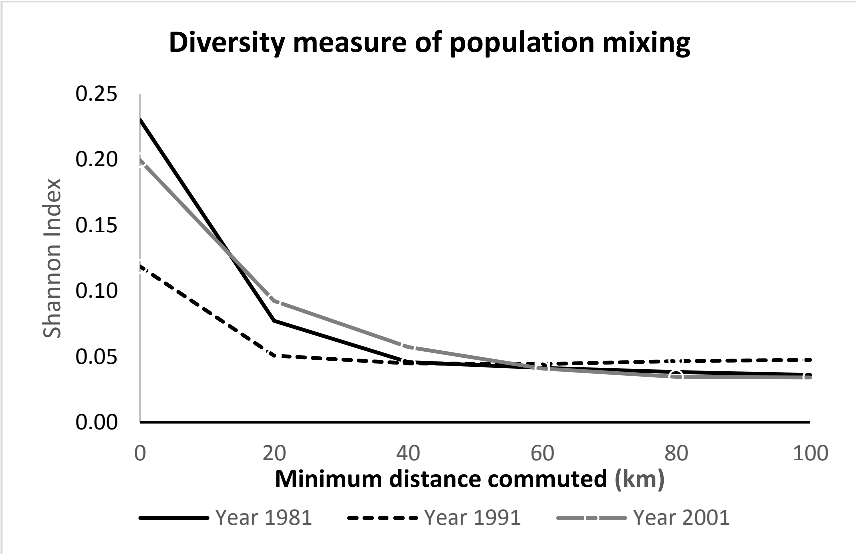
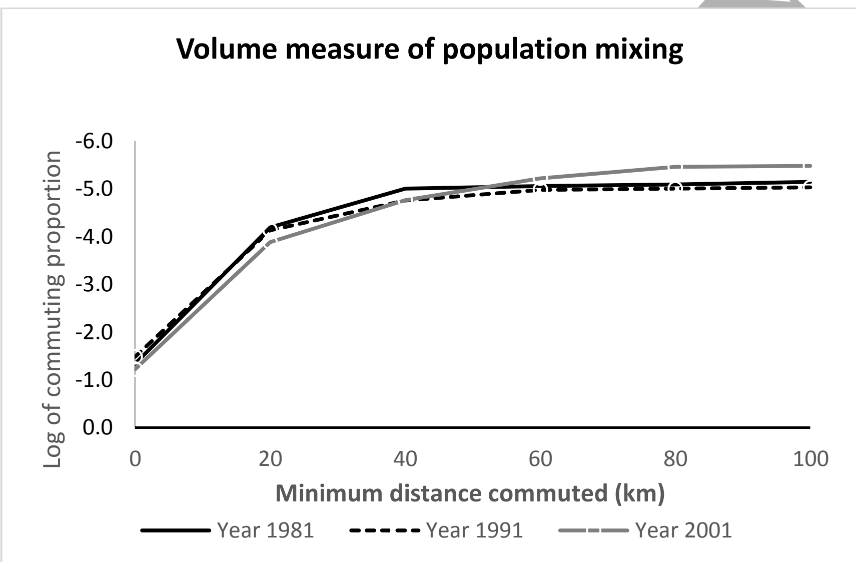


Figure 5. Population mixing due to commuting: Seascale.Note that there were data issues for 1991 – so this year was not presented. These issues related to the published intra-ward flows being based on a 10% sample and subjected to data blurring which resulted in

a matrix too sparse and unreliable to allow meaningful analysis (see Materials and Methods section).





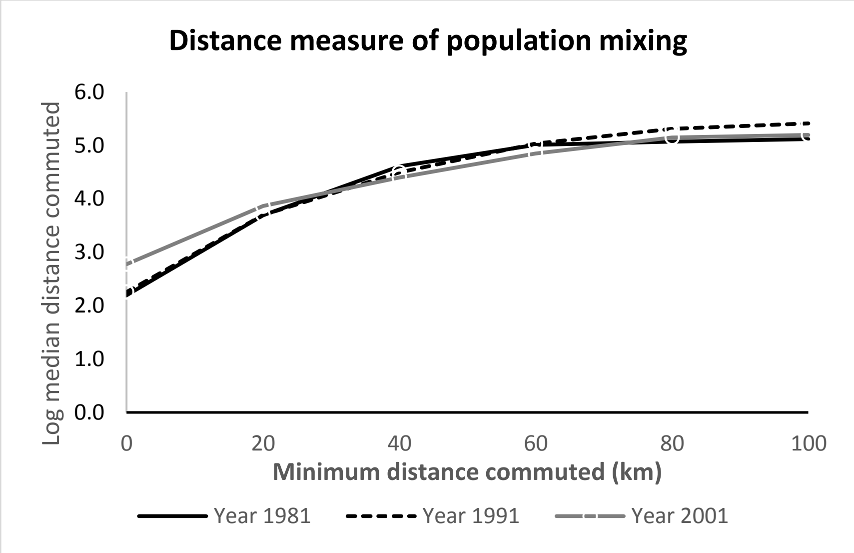
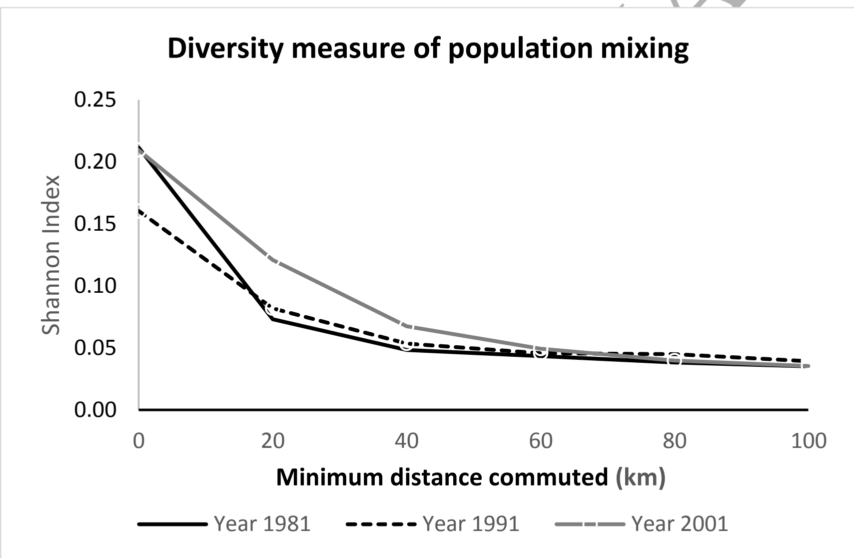
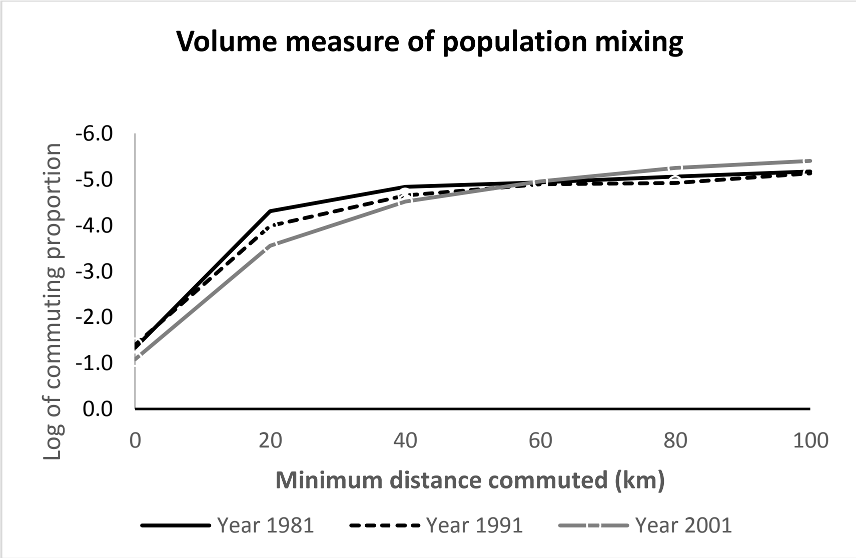


Figure 6. Population mixing due to commuting: Allerdale plus Copeland without Seascale.Mean value reported for diversity and volume and median for distance measure. These larger areas were not affected in the same way as wards noted above.





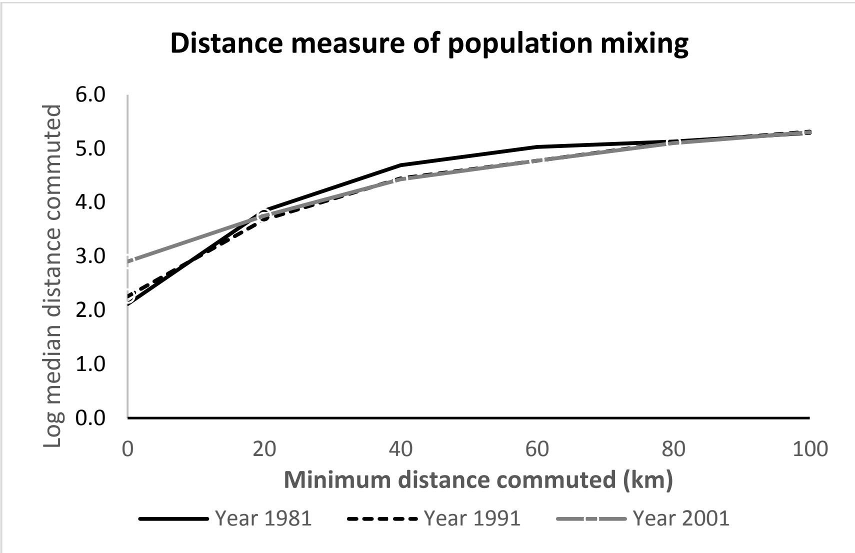


Figure 7. Population mixing due to commuting: Cumbria without Seascale. Mean value reported for diversity and volume and median for distance measure. These larger areas were not affected in the same way as wards noted above.