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EN MEDICINA CLÍNICA Y SALUD PÚBLICA

**Impacto de las desigualdades
socioeconómicas en los principales
indicadores epidemiológicos del
cáncer en España**

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*No aman de igual forma
los ricos y los pobres.*

*Los pobres aman con todo en su contra,
sin bonitos decorados.
Entienden de lunes y de tedios domingueros
y de gastos imprevistos,
de facturas y de angustias
que embisten
mes a mes
a quemarropa.*

*Los pobres han aprendido
a amarse a oscuras,
mal alimentados
mal vestidos, malqueridos,
y en sus jardines también crecen las flores
(aunque no haya jardines).*

Gata Cattana

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Siglas y abreviaturas:

- AECC: Asociación Española Contra el Cáncer.
- ASR: Age-Standardised Rate (tasa estandarizada por edad).
- ASR-E: Tasa estandarizada por edad por la población europea.
- ASR-W: Tasa estandarizada por edad por la población mundial.
- ECIS: European Cancer Information System.
- ENCR: European Network of Cancer Registries.
- GCO: Global Cancer Observatory.
- IACR: International Association of Cancer Registries.
- IARC: International Agency for Research on Cancer.
- IC: Intervalo de confianza.
- INE: Instituto Nacional de Estadística.
- JCR: Journal Citation Reports.
- OMS: Organización Mundial de la Salud.
- RCBP: Registro de Cáncer de Base Poblacional.
- RCG: Registro de Cáncer de Granada.
- REDECAN: Red Española de Registros de Cáncer.
- SN: Supervivencia neta.
- SO: Supervivencia observada.
- TB: Tasa bruta.
- TEE: Tasa específica por edad.

Resumen

Introducción: El cáncer es un grave problema de salud pública, siendo los cánceres de pulmón, mama y colon-recto los más frecuentes en términos de incidencia y mortalidad. Se sabe que el nivel socioeconómico es un factor que puede influir de manera determinante en los principales indicadores epidemiológicos del cáncer. En España, la evidencia científica sobre el impacto de las desigualdades socioeconómicas en el cáncer es limitada.

Metodología: Se elaboró una revisión de revisiones sistemáticas sobre desigualdades socioeconómicas en cáncer de pulmón. Además, se realizaron 3 estudios pioneros en España sobre el impacto del nivel socioeconómico en la esperanza de vida, en la incidencia de los cánceres de pulmón, mama y colon-recto, y en la mortalidad por cáncer de pulmón. Para medir el nivel socioeconómico se utilizó un indicador de área a nivel de sección censal.

Resultados: La revisión mostró que las personas de nivel socioeconómico más bajo tienen más riesgo de desarrollar y morir por un cáncer de pulmón, así como una menor supervivencia. Esto puede estar relacionado principalmente con el tipo de tratamientos que reciben, en comparación con pacientes de nivel socioeconómico más alto.

En España, la esperanza de vida es mayor en hombres y mujeres de nivel socioeconómico más alto, que viven 3,8 y 3,2 años más, respectivamente, que los de nivel socioeconómico más bajo. Además, existen importantes desigualdades socioeconómicas en la incidencia y la mortalidad de los cánceres de pulmón, colon-recto y mama en España. Un nivel socioeconómico más bajo se asoció con una mayor incidencia y mortalidad de cáncer de pulmón en hombres. Por el contrario, las mujeres de nivel socioeconómico más alto tuvieron una mayor incidencia y mortalidad de cáncer de mama y pulmón. Para el cáncer de colon-recto, se encontró una mayor incidencia entre hombres de nivel socioeconómico más alto.

Conclusiones: El nivel socioeconómico influye en los principales indicadores epidemiológicos de los cánceres de pulmón, colon-recto y mama en España. Es necesario profundizar en las causas subyacentes de estas diferencias para poder implementar políticas de salud pública enfocadas a reducir las desigualdades.

Abstract

Introduction: Cancer is a major public health problem, with lung, breast and colorectal cancers being the most frequent in terms of incidence and mortality. Socioeconomic status is a factor that can decisively influence the main epidemiological indicators of cancer. In Spain, scientific evidence on the impact of socioeconomic inequalities in cancer is limited.

Methods: We conducted an overview of systematic reviews (umbrella review) on socioeconomic inequalities in lung cancer outcomes. In addition, 3 pioneering studies were carried out in Spain on the impact of socioeconomic status on life expectancy, on lung, breast and colorectal cancer incidence, and on lung cancer mortality. To measure socioeconomic status, an area indicator was used at the census tract level.

Results: The umbrella review showed that people of lower socioeconomic status have a higher risk of developing and dying from lung cancer, as well as lower survival. This can be mainly related to the type of treatments they receive, compared to patients of higher socioeconomic status.

In Spain, life expectancy is higher in men and women of higher socioeconomic status, who live 3.8 and 3.2 years longer, respectively, than those of lower socioeconomic status. Furthermore, there are important socioeconomic inequalities in the incidence and mortality of lung, colorectal and breast cancers in Spain. Lower socioeconomic status was associated with higher lung cancer incidence and mortality in men. On the contrary, women of higher socioeconomic status had a higher incidence and mortality of breast and lung cancer. For colorectal cancer, a higher incidence was found among men of higher socioeconomic status.

Conclusions: Socioeconomic status influences the main epidemiological indicators of lung, colorectal and breast cancer in Spain. It is necessary to investigate the underlying causes in order to implement public health policies focused on reducing these inequalities.

Introducción

1.1. El cáncer y sus causas

El cáncer no es una única enfermedad, sino un conjunto de enfermedades en las cuales las células del cuerpo comienzan a crecer y multiplicarse de forma anormal, formando masas de tejido, más o menos diferenciadas, que pueden invadir y dañar tejidos circundantes [1]. Casi cualquier parte del cuerpo humano, que está formado por unas $3 \cdot 10^{13}$ células [2], puede desarrollar cáncer. Por ello, aunque hablemos del cáncer como una única enfermedad, en realidad hay más de 200 tipos distintos de cáncer con diferentes características.

Las causas del cáncer también son diversas, siendo el proceso de aparición complejo y multifactorial [3]. A menudo el causante del cáncer no es un solo factor, sino la combinación e interacción de distintos factores ambientales y genéticos [3]. Los factores ambientales son la causa del cáncer en un 90-95 % de los casos, mientras que la genética es responsable del restante 5-10 %, si bien estos porcentajes pueden variar en función del tipo de cáncer [4, 5].

Los factores causantes del cáncer se pueden clasificar principalmente en dos categorías: factores no modificables (factores sobre los que no tenemos ningún control) y factores modificables (en donde se centra la prevención primaria del cáncer).

Factores no modificables son por ejemplo:

- Edad. La edad es el principal factor de riesgo del cáncer. En gene-

ral, el cáncer aumenta con la edad, aunque algunos cánceres son más frecuentes en niños o adolescentes [6].

- Sexo. En general, el cáncer suele ser más frecuente en hombres que en mujeres [6].
- Raza o etnia. Si bien no existe una definición consensuada de estos términos en la investigación en salud [7], están documentadas diferencias importantes en las características del cáncer en función de la raza o etnia [8, 9].
- Historia familiar, en algunas localizaciones anatómicas como mama, ovario, colon... [10].
- Enfermedades genéticas, como el síndrome de Lynch y su relación con el cáncer colorrectal [11].

Factores modificables pueden ser:

- Consumo de tabaco. El tabaco aumenta el riesgo de incidencia de algunos tipos de cáncer entre 10 y 20 veces más. En 2020, la Organización Mundial de la Salud (OMS) estimó en 1.000 millones los fumadores de tabaco mayores de 15 años, a los que hay que añadir 24 millones de niños de entre 13 y 15 años que consumen tabaco [12]. Si bien las tasas de tabaquismo están descendiendo a nivel global, los fumadores pasivos y la emergente presencia de sistemas electrónicos de administración de nicotina, como los cigarrillos electrónicos o el tabaco calentado, son problemas de salud pública preocupantes [12].
- Consumo de alcohol. Junto al consumo de tabaco, son los principales factores de riesgo modificables del cáncer [13]. El consumo de alcohol se asocia con una mayor incidencia de cáncer de cavidad oral, orofaringe, esófago, hígado, mama y colon-recto [14]. No existe un nivel seguro de consumo de alcohol para el cáncer y todos los tipos de bebidas alcohólicas están relacionadas con un aumento del cáncer [14].
- Dieta, sedentarismo y peso corporal. Para prevenir el cáncer es importante llevar una dieta equilibrada, realizar actividad física y evitar el sobrepeso y la obesidad. El exceso de peso se ha relacionado con hasta 13 tipos de cáncer [15, 16] y es la causa de entre el 4% y el 38%

de algunos cánceres como esófago, colon-recto, vesícula biliar, mama en mujeres postmenopáusicas, endometrio, ovario, riñón y cáncer de próstata avanzado [17].

- Exposición solar. Debe controlarse para disminuir el riesgo de melanoma y otros tumores de la piel.
- Exposición a distintos carcinógenos (agentes que producen cáncer) químicos y físicos diferentes a los anteriores. La Agencia Internacional para la Investigación en Cáncer (IARC, por sus siglas en inglés: *International Agency for Research on Cancer*) tiene registrados 120 agentes (químicos, metales, radiaciones, productos farmacéuticos...) que producen cáncer en humanos [18], si bien el tipo de cáncer depende del tipo de exposición, su intensidad y el tiempo de exposición [19].

El Código Europeo Contra el Cáncer [20], desarrollado por la IARC, recoge en su 4^a edición doce formas para reducir el riesgo de cáncer modificando la exposición a los factores modificables del cáncer y participando en programas de cribado de cáncer de mama, colon-recto y cuello uterino.

Existen otros factores que no se pueden clasificar como modificables ni como no modificables, ya que algunos de sus aspectos no se pueden cambiar fácilmente a nivel individual y menos si se tiene en cuenta que trabajamos con patologías en el que el periodo de inducción suele ser habitualmente bastante prolongado en el tiempo. Entre estos factores se encuentran los factores socioeconómicos, que se corresponden con aquellas características del sujeto que vienen condicionadas por su interacción con su entorno, tales como su nivel educativo, nivel de renta, nivel socioeconómico, grado de cobertura sanitaria y lugar de residencia.

1.2. Impacto del cáncer en la población: un problema de salud pública

El cáncer es en la actualidad uno de los mayores problemas de salud pública a nivel mundial. En el año 2020, según las estimaciones del *Global Cancer*

Observatory (GCO), se diagnosticaron en el mundo 18,1 millones de casos nuevos de cáncer y se produjeron 9,9 millones defunciones por cáncer [6]. El cáncer de mama fue el más diagnosticado (12,5 % del total de casos) y el cáncer de pulmón fue la principal causa de muerte por cáncer (18,2 % del total de defunciones) [6]. A nivel mundial, se estimó que 4 de cada 10 hombres y 3 de cada 10 mujeres desarrollarán algún tipo de cáncer (excepto cáncer de piel no melanoma) antes de los 75 años de edad [6]. Existen importantes variaciones geográficas en la distribución del cáncer en el mundo, debidas principalmente a las diferencias en estilos de vida y al contexto económico y sanitario entre las diferentes regiones [21].

En Europa, durante el año 2020 se han diagnosticado 4 millones de casos de cáncer (exceptuando el cáncer de piel no melanoma) y se han producido 1,9 millones de defunciones por cáncer [22].

Los últimos datos de incidencia disponibles para España son del año 2023, donde se estima que más de 279.000 personas serán diagnosticadas de cáncer a lo largo del año [23]. Frente a estas estimaciones, las cifras reales de mortalidad indican que en el año 2020 se produjeron más de 111.000 defunciones por cáncer en España [24]. En el conjunto de la población, el cáncer más frecuente es el de colon y recto con un total de 42.721 nuevos casos (28.465 de colon y 14.256 de recto) [23]. Le siguen el cáncer de mama en mujeres con 35.001 casos nuevos, el cáncer de pulmón con 31.282 y el de próstata con 29.002 [23].

Además de la magnitud del cáncer a nivel epidemiológico, es relevante considerar la perspectiva del impacto económico y social de la enfermedad. En el año 2020, la Asociación Española Contra el Cáncer (AECC) estimó en 19.300 millones de euros el coste a la sociedad del cáncer, teniendo en cuenta costes directos médicos (derivados del tratamiento o el seguimiento de la enfermedad), costes directos no médicos (como transporte, obras o cuidados) y costes indirectos (pérdida de ingresos tras el cáncer y pérdida de productividad por muertes prematuras) [25].

Por otro lado, la línea de investigación que se desarrolla en esta tesis doctoral sigue uno de los ejes principales de la Misión Cáncer [26], una de las 5 misiones que pone en marcha la Comisión Europea en 2021 y que continúa actualmente. En concreto, uno de sus objetivos es el de garantizar el acceso equitativo al diagnóstico y el tratamiento, reconociendo que existen importantes desigualdades.

A la vista de estos datos, podemos afirmar que el estudio del cáncer en todas sus vertientes es necesario para reducir el impacto de la enfermedad en la población, mediante acciones como la planificación de la atención sanitaria, la evaluación de la efectividad de sus tratamientos o el desarrollo de estrategias de prevención como la prevención primaria y los programas de cribado.

1.3. Principales indicadores epidemiológicos del cáncer en la población

Para medir el impacto del cáncer en la población se utilizan principalmente cuatro indicadores:

- **Incidencia** (casos nuevos). Indica el riesgo de ser diagnosticado de cáncer.
- **Mortalidad** (defunciones). Indica el riesgo de morir por cáncer.
- **Supervivencia** (porcentaje de casos vivos). Indica la historia natural del cáncer y la efectividad del tratamiento.
- **Prevalencia** (casos que continúan vivos). Indica la carga asistencial de la enfermedad.

Estos indicadores son clave para la vigilancia epidemiológica y el control del cáncer, las actividades de prevención y la planificación de la asistencia sanitaria.

1.3.1. Indicadores para la incidencia

Número de casos

La medida básica para medir la incidencia de cáncer es el número de casos nuevos, que se corresponde realmente con el número de casos nuevos diagnosticados. A partir de este indicador, se calculan otros más complejos que proporcionan distinta información sobre la incidencia de la enfermedad.

Tasa bruta

La tasa bruta (TB) por 100.000 habitantes para un periodo concreto se define como el cociente entre el número de casos nuevos y el número de personas-año a riesgo por 100.000 [27]. El número de personas-año a riesgo es la población que podría haber sido diagnosticada de cáncer y en general se calcula como la suma de la población año a año.

$$TB = \frac{\text{Número de casos nuevos}}{\text{Personas-año a riesgo}} \cdot 100.000 = \frac{N}{P} \cdot 100.000$$

Las tasas brutas se usan muy a menudo debido que su cálculo es sencillo y son fácilmente interpretables, aunque pueden enmascarar diferencias existentes entre grupos de edad [28]. Para analizar la incidencia en distintas edades, se utilizan las tasas específicas por edad.

Tasa específica por edad

La tasa específica por edad se define como la tasa bruta para un grupo de edad específico [27]. Esto es, la tasa específica por edad para el grupo de 30 a 34 años se calcula dividiendo el número de casos nuevos ocurridos en personas de 30 a 34 años entre el número de personas-año en ese mismo rango de edad.

Aunque las tasas específicas se pueden calcular para cualquier rango de edad, es común que se representen por grupos de edad quinquenales. En ocasiones

puede resultar de interés analizar por separado los indicadores para niños menores de 1 año, que pueden tener características diferentes al resto de niños, y agrupar a los mayores de una determinada edad avanzada en un solo grupo de edad. Es por ello que, en general, las tasas específicas por edad se suelen calcular en 18 grupos de edad (0-4 años, 5-9, ..., 80-84, 85 años y más), 19 grupos de edad (0, 1-4, 5-9, ..., 80-84, 85 y más) ó 21 grupos de edad (0, 1-4, 5-9, ..., 80-84, 85-89, 90-94, 95 y más).

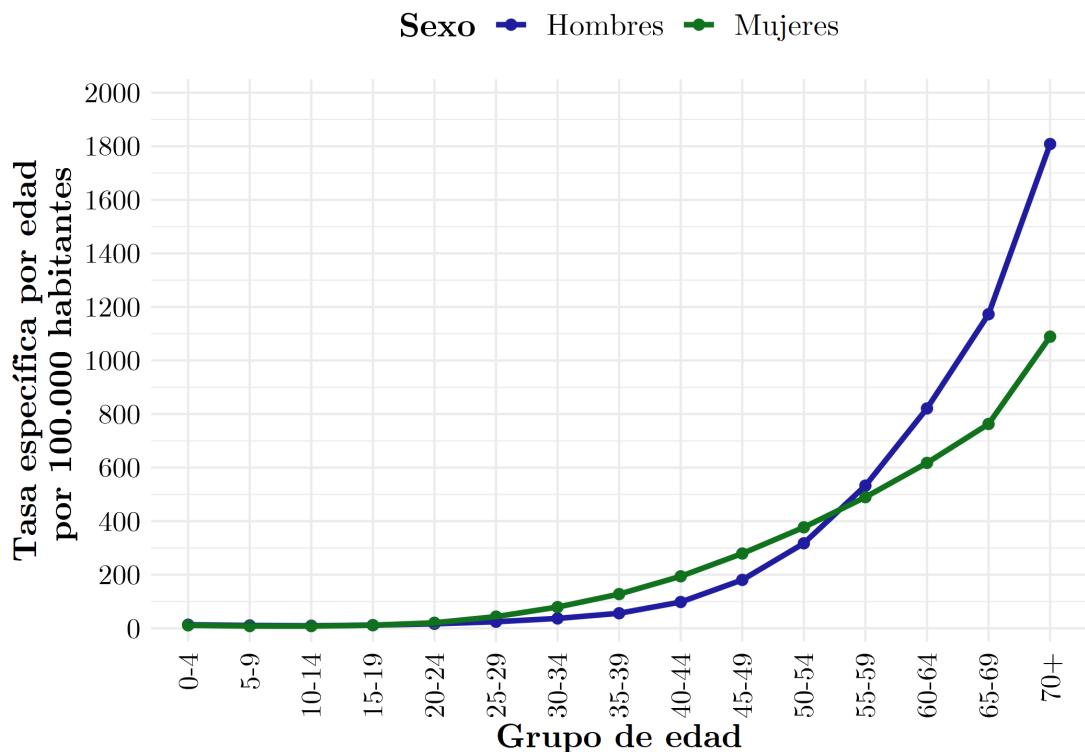
La tasa específica por edad (TEE) para el i -ésimo grupo de edad viene dada por la siguiente fórmula:

$$\text{TEE}_i = \frac{N_i}{P_i} \cdot 100.000$$

donde N_i indica el número de casos nuevos ocurridos en el i -ésimo grupo de edad y P_i indica las personas-año en el i -ésimo grupo de edad.

En la Figura 1 se representan las TEE de incidencia del total del cáncer excepto piel no melanoma por sexo en el mundo para el año 2020.

Figura 1. Tasas específicas de incidencia del total del cáncer (excepto piel no melanoma) por edad y sexo en el mundo, 2020.



Fuente: Cancer Today, Global Cancer Observatory (GCO) [6].

La incidencia de cáncer aumenta exponencialmente con la edad [6]. De los 20 a los 54 años, las tasas específicas por edad en mujeres son mayores que en hombres, debido principalmente a la magnitud del cáncer de mama en las mujeres premenopáusicas. En la infancia y adolescencia (0-19 años) y a partir de los 55 años, la incidencia de cáncer siempre es mayor en hombres que en mujeres.

Tasa estandarizada por edad

Exceptuando algunos cánceres que son más frecuentes en niños o personas jóvenes, en general la frecuencia del cáncer aumenta con la edad. Este hecho hace que la comparación de tasas brutas entre diferentes poblaciones (o incluso entre la misma población en distintos períodos de tiempo) no sea

factible, dadas las diferencias en la estructura etaria de la población [29]. Esto es, si una población fuese mucho más joven que otra, incluso aunque las tasas específicas por edad fuesen iguales en ambas poblaciones, se diagnosticarían más casos en la población más anciana. Para resolver este inconveniente surgen las tasas estandarizadas por edad (ASR, por sus siglas en inglés: *Age-Standardised Rate*).

Las tasas estandarizadas por edad son las tasas de incidencia que observaríamos en la población de estudio si esa población tuviese exactamente la misma estructura de edad que la población estándar predefinida [27]. Una población estándar consiste en la distribución de 100.000 habitantes ficticios en grupos de edad (generalmente, 18, 19 ó 21 grupos de edad tal y como se ha descrito previamente). Esta distribución teórica intenta reflejar el comportamiento de un determinado problema de salud-enfermedad en un área geográfica, permitiendo la comparabilidad de tasas estandarizadas entre distintas regiones. El método más frecuente y recomendado de obtención de tasas estandarizadas por edad es el llamado “método directo”, también conocido como de la “población tipo” [30].

En la práctica, para el cálculo de una tasa estandarizada por edad según el método directo se calculan primero las tasas específicas por edad. A continuación, la tasa de cada grupo de edad es multiplicada por un peso, que consiste en dividir entre 100.000 la población estándar de ese grupo de edad. Para N grupos de edad, la fórmula para obtener la tasa estandarizada por edad es:

$$\text{ASR} = \sum_{i=1}^N \text{PE}_i \cdot \text{TEE}_i$$

donde TEE_i es la tasa específica por edad del i -ésimo grupo de edad y PE_i es la población estándar para el i -ésimo grupo de edad.

Las poblaciones estándar más utilizadas son:

- Población estándar mundial (1960). Propuesta por primera vez por Segi [31] en 1960 y modificada más tarde por Doll et al. [32] en 1966.
- Antigua población estándar europea (1976). Propuesta en 1976 por

Waterhouse et al. [33] basándose en la estructura de edad de varias poblaciones escandinavas.

- Nueva población estándar europea (2013). Revisión de la población estándar europea de 1976 por parte de la Oficina Europea de Estadística (EUROSTAT) [34]. Esta nueva población estándar representa mejor el envejecimiento de la población europea. El uso de esta población estándar aún no está ampliamente extendido, aunque se espera que en unos años sustituya completamente a su predecesora. Además de redistribuir el peso de los determinados grupos de edad de la población estándar europea de 1976, permite la posibilidad de ampliar el número de grupos de edad a 21, añadiendo los grupos de edad de 90-94 años y ≥ 95 años, adaptándose al incremento de habitantes de avanzada edad por el aumento de la esperanza de vida.

Otros indicadores

Existen otros indicadores epidemiológicos que miden distintos aspectos de la incidencia, como son las tasas truncadas o las tasas acumulativas [27].

1.3.2. Indicadores para la mortalidad

Para la mortalidad, se pueden calcular de forma similar las mismas tasas que calculamos para la incidencia, cambiando el número de casos incidentes por el número de defunciones por cáncer.

Es importante señalar que una defunción por cáncer se define como una muerte que es causada directamente por el cáncer. Por tanto, una defunción por cáncer no debe confundirse con defunciones de personas que tienen cáncer pero fallecen por otras causas (como un infarto agudo de miocardio, un accidente de tráfico o cualquier otra causa).

1.3.3. Indicadores para la supervivencia

La supervivencia suele expresar el porcentaje de pacientes vivos tras un periodo de tiempo determinado (normalmente 1, 3 ó 5 años). Para el cálculo de la supervivencia es necesario un seguimiento del estado vital de los casos de cáncer para determinar el tiempo que transcurre desde el diagnóstico hasta que mueren, son perdidos en el seguimiento o siguen vivos al final del periodo considerado.

Existen, principalmente, dos tipos de indicadores epidemiológicos para medir la supervivencia:

Supervivencia observada

La supervivencia observada (o global) mide el tiempo transcurrido desde el diagnóstico de un paciente de cáncer hasta su fallecimiento por cualquier causa [35]. La supervivencia observada es una medida muy simple, fácil de calcular e interpretar. No obstante, este indicador no refleja de forma real la probabilidad de fallecimiento atribuible al cáncer, dado que los pacientes también fallecen por otras causas de mortalidad que actúan como riesgos competitivos del cáncer.

Supervivencia neta

Como respuesta a la debilidad anteriormente mencionada de la supervivencia observada, surge otro indicador epidemiológico: la supervivencia neta. La supervivencia neta representa la probabilidad de sobrevivir al cáncer en el hipotético caso de que ese cáncer fuera la única causa posible de defunción [35]. Para el cálculo de la supervivencia neta se usa un método analítico para eliminar las probabilidades de fallecimiento por el resto de posibles causas de muerte.

La principal herramienta para el cálculo de la supervivencia neta son las tablas de vida, que miden la mortalidad general y la esperanza de vida de una población para cada valor de una serie de variables como sexo, año y

edad [35–37].

Además, de forma similar a lo que ocurre con la incidencia y la mortalidad, es posible la estandarización por edad de la supervivencia neta [38]. Esta estandarización permite las comparaciones de supervivencia con otras áreas geográficas o períodos, ya que reduce el efecto de las posibles diferencias en la estructura de edad de esas poblaciones, las cuales pueden tener una gran influencia en el resultado de la supervivencia.

Existen otros indicadores que miden la supervivencia, como la supervivencia libre de enfermedad, que consiste en el periodo de tiempo en el que un paciente no muestra signos de que la enfermedad haya progresado o regresado tras un tratamiento del cáncer.

1.3.4. Indicadores para la prevalencia

Los principales indicadores para medir la prevalencia son el número de casos de cáncer prevalentes (esto es, casos tanto nuevos como antiguos que siguen vivos) y la proporción por cada 100.000 habitantes [6]. Al igual que para la supervivencia, se suelen reportar estos indicadores a 1, 3 y 5 años.

1.4. Registros de Cáncer de Base Poblacional

Para conocer la carga real de incidencia de cáncer en una población determinada es necesario disponer de un Registro de Cáncer de Base Poblacional (RCBP). Es decir, de un sistema de información en el que se recogen, analizan e interpretan datos sobre todas las personas diagnosticadas de cáncer en un área geográfica bien definida. La exhaustividad debe ser un requisito indispensable de los RCBP.

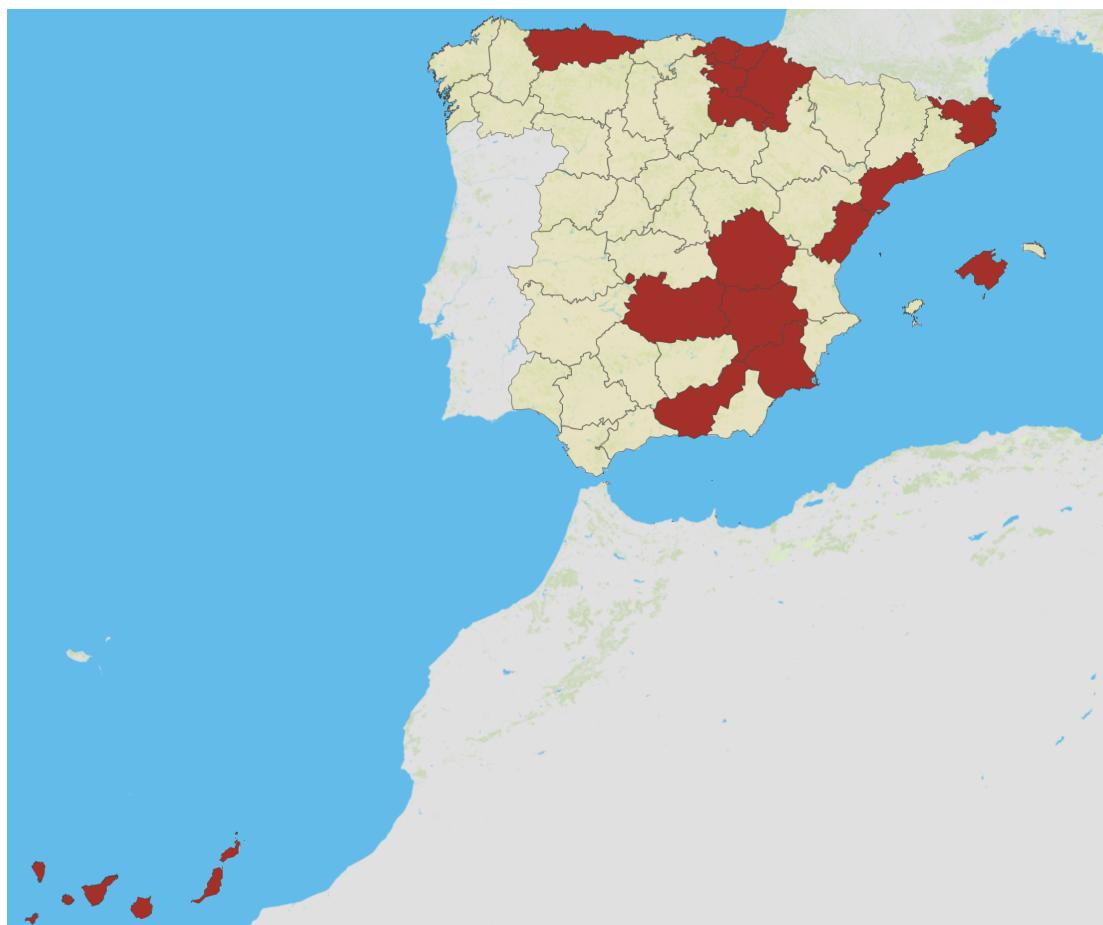
1.4.1. Situación global de los Registros de Cáncer de Base Poblacional en España

En algunos países como Australia, Dinamarca, Suecia o Canadá existen RCBP nacionales, que cubren a la totalidad de la población del país. En otros países sólo existen RCBP regionales. Es el caso de España, donde los RCBP cubren en la actualidad aproximadamente el 27 % de la población nacional. En algunos países menos desarrollados de Asia o África (Bangladesh, Angola...) no existe ningún Registro sobre la incidencia de cáncer.

Cancer Incidence in Five Continents [39] es la mayor publicación sobre datos observados en RCBP de todo el mundo y recoge en su undécimo y último volumen datos del periodo 2008-2012 de 343 registros en 65 países. La publicación de los datos de incidencia de cáncer en este volumen es un sinónimo de calidad en el registro de casos que realiza el RCBP.

En el último volumen disponible de *Cancer Incidence in Five Continents* (vol. XI) [39] han publicado sus datos 14 RBCP españoles: Albacete, Asturias, Castellón, Ciudad Real, Cuenca, Girona, Granada, Islas Canarias, La Rioja, Mallorca, Murcia, Navarra, País Vasco y Tarragona (Figura 2).

Figura 2. Regiones de España cubiertas por los Registros de Cáncer de Base Poblacional que han publicado sus datos en el volumen XI de *Cancer Incidence in Five Continents*.



Fuente: Mapa de elaboración propia

1.4.2. El Registro de Cáncer de Granada

El Registro de Cáncer de Granada (RCG) es un RCBP que surge como un proyecto de la Consejería de Salud y Consumo de la Junta de Andalucía, adscrito para su desarrollo a la Escuela Andaluza de Salud Pública.

El RCG es uno de los Registros con más antigüedad de España. Inicia su actividad en el año 1985, cubriendo desde entonces la totalidad de la provin-

cia de Granada, que cuenta en 2023 con una población de aproximadamente 934.000 habitantes [40]. El RCG está integrado y participa desde su creación, en la *International Agency for Research on Cancer* (IARC), la *International Association of Cancer Registries* (IACR) y la *European Network of Cancer Registries* (ENCR). Además, desde el año 2010 forma parte de la Red Española de Registros de Cáncer (REDECAN).

El RCG es el único Registro de Cáncer de Andalucía acreditado por la IARC, institución perteneciente a la OMS. En el año 2007 se crea y regula el Registro de Cáncer de Andalucía (Decreto 297/2007 del Boletín Oficial de la Junta de Andalucía), adscrito a la actual Dirección General de Salud Pública y Ordenación Farmacéutica de la Consejería de Salud y Consumo de la Junta de Andalucía e integrado por registros establecidos en cada una de las provincias andaluzas. El RCG se incorpora al Registro de Cáncer de Andalucía tras su creación. Posteriormente, se publica el Decreto 586/2019, por el que se regula el Registro de Cáncer de Andalucía.

En el RCG se utilizan normas y procedimientos de trabajo homologados a nivel internacional, lo que permite asegurar la calidad de la información, así como comparar los resultados con otros registros de cáncer de población. Los datos de incidencia del RCG cumplen con los estándares internacionales de calidad y por ello se han publicado en *Cancer Incidence in Five Continents*, desde el volumen VI (publicado en 1992) [41] hasta el último volumen disponible hasta la fecha, el volumen XI (publicado en 2017) [39]. Además, la incidencia registrada por el RCG ha sido utilizada para realizar estimaciones de incidencia de cáncer a nivel nacional [23, 42, 43], a nivel europeo [22] y a nivel mundial [6, 21]. En esta tesis doctoral se van a utilizar datos de RCBP nacionales como el RCG, que cuentan con altos niveles de calidad.

Para cumplir con la calidad y exhaustividad requerida, el RCG se nutre de diversas fuentes de información para asegurar la recogida de todos los casos incidentes de cáncer de la provincia. Entre sus fuentes de información, destacan las siguientes:

- Todos los hospitales públicos y privados de la provincia:

- Hospital Universitario Virgen de las Nieves.
 - Hospital Universitario Clínico San Cecilio.
 - Hospital de Alta Resolución de Loja.
 - Hospital de Alta Resolución de Guadix.
 - Hospital de Baza.
 - Hospital Santa Ana de Motril.
 - Hospital HLA Inmaculada.
 - Hospital Vithas La Salud.
 - Hospital de San Rafael.
- Laboratorios privados de Anatomía Patológica.
- Laboratorios de Hematología y Hemoterapia.
- Registro de Mortalidad de Andalucía.

En la actualidad, el RCG tiene registrados desde su creación más de 145.000 casos nuevos de cáncer en la provincia. Como característica singular, se debe destacar que el RCG incluye los casos de cáncer de piel no melanoma (un tipo de cáncer muy frecuente pero con buen pronóstico). Esto es un hecho poco frecuente entre los RCBP debido a la gran carga de trabajo que lleva ese registro y a la dificultad de disponer de datos exhaustivos.

En la figura 3 se muestra la ficha de Registro del RCG, con toda la información que se recoge de cada caso incidente de cáncer, dividida en tres apartados principales: datos personales, datos del tumor y fuentes de información.

Figura 3. Ficha del Registro de Cáncer de Granada donde se recoge la información de cada caso incidente de cáncer.

|  Junta de Andalucía Consejería de Salud y Consumo Escuela Andaluza de Salud Pública | | REGISTRO DE CÁNCER DE GRANADA | | NUM. DE REGISTRO <input type="text"/> | NUM. PREVIO <input type="text"/> | |
|--|---|--------------------------------------|--|---------------------------------------|---|---------------------------|
| <small>P E R D S A O T N O S L E S</small> <small>D E L A T U M S O R</small> <small>F U E N T E S</small> | Apellidos y nombre NUHSA <input type="text"/> Nº Seguridad Social <input type="text"/> DNI/NIE <input type="text"/> Sexo <input type="checkbox"/> Lugar de nacimiento (municipio y provincia) Residencia habitual: calle y número municipio y provincia <input type="text"/> | | | | | |
| | Localización PREVIO Localización <input type="text"/> Fecha de incidencia <input type="text"/> Fecha DAP <input type="text"/> Diagnóstico anatomo-patológico <input type="text"/> Base del diagnóstico cT <input type="text"/> N <input type="text"/> M <input type="text"/> Neoady <input type="checkbox"/> pT <input type="text"/> N <input type="text"/> M <input type="text"/> Ganglios (+/exam.) <input type="text"/> Extensión <input type="checkbox"/> Estadio <input type="text"/> Breslow <input type="text"/> Clark <input type="checkbox"/> Gleason <input type="text"/> | | | | | Edad <input type="text"/> |
| | Otras neoplasias primarias Último contacto (fecha/motivo/fuente) Fecha de fallecimiento/Registro Civil | | | | | <input type="text"/> |
| Fuentes (centros y servicios) y nº de historia clínica: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | | | | | Fecha de primera información <input type="text"/> | |
| Observaciones: <input type="text"/> | | | | | | |

1.5. Impacto del cáncer de pulmón, mama y colon-recto

1.5.1. Incidencia

Los cánceres de pulmón, mama y colon-recto son los tres tipos de cáncer más frecuentes en el mundo en ambos sexos, según datos del 2020 [6], representando el 35,4 % del total de todos los casos de cáncer. En la tabla 1 se muestra la incidencia estimada de cáncer para los cánceres de pulmón, mama y colon-recto a nivel español (proporcionadas por REDECAN [23]), europeo (realizadas por el *European Cancer Information System*, ECIS, de

la Comisión Europea [22]) y mundial (calculadas por el GCO de la OMS [6]). Se presentan las últimas estimaciones de incidencia disponibles hasta la fecha, que son para 2020 en Europa y el mundo y para 2023 en España.

Respecto al cáncer de mama, el cáncer de mama en hombres es una enfermedad rara que representa aproximadamente 1 de cada 100 casos de cáncer de mama en mujeres [44]. Al ser un cáncer con una baja incidencia, no se suele incluir en las principales estimaciones de indicadores epidemiológicos que se realizan a nivel español [23], europeo [22] o mundial [6].

Tabla 1. Incidencia estimada para España, Europa y el mundo de los cánceres de pulmón, mama y colon-recto por sexo. Número de casos estimados, tasa bruta por 100.000 habitantes, tasa estandarizada por la población mundial por 100.000 habitantes y ranking de tipos de cáncer más incidentes.

| Sexo | Localización anatómica | Contexto | N | TB | ASR-W | R |
|----------------|------------------------|--------------|-----------|-------|-------|----|
| Hombres | Pulmón | España, 2023 | 22.266 | 95,4 | 42,6 | 3º |
| | | Europa, 2020 | 315.054 | 87,1 | 43,6 | 2º |
| | | Mundo, 2020 | 1.435.943 | 36,5 | 31,5 | 1º |
| | Colon-recto | España, 2023 | 26.357 | 112,9 | 49,5 | 2º |
| | | Europa, 2020 | 281.714 | 77,9 | 37,9 | 3º |
| | | Mundo, 2020 | 1.065.960 | 27,1 | 23,4 | 3º |
| Mujeres | Pulmón | España, 2023 | 9.016 | 37,0 | 17,1 | 3º |
| | | Europa, 2020 | 162.480 | 42,0 | 18,1 | 3º |
| | | Mundo, 2020 | 770.828 | 19,9 | 14,6 | 3º |
| | Mama | España, 2023 | 35.001 | 143,7 | 77,1 | 1º |
| | | Europa, 2020 | 531.086 | 137,2 | 74,3 | 1º |
| | | Mundo, 2020 | 2.261.419 | 58,5 | 47,8 | 1º |
| | Colon-recto | España, 2023 | 16.364 | 67,2 | 26,4 | 2º |
| | | Europa, 2020 | 238.106 | 61,5 | 24,6 | 2º |
| | | Mundo, 2020 | 865.630 | 22,4 | 16,2 | 2º |

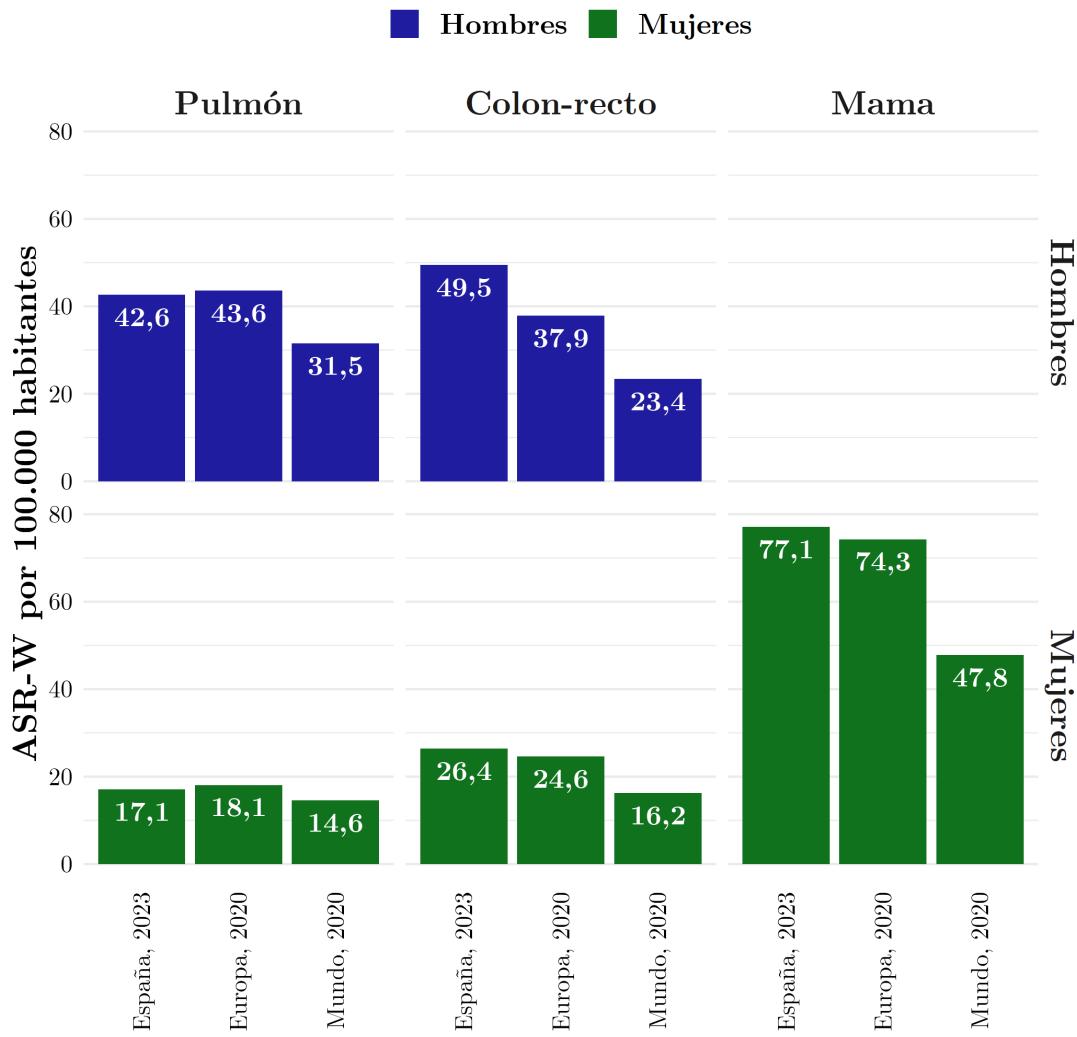
N: Número de casos estimados; TB: Tasa bruta por 100.000 habitantes; ASR-W: Tasa estandarizada por la población mundial por 100.000 habitantes; R: Ranking de tipos de cáncer más incidentes.

Los cánceres de pulmón y colon-recto son más frecuentes en hombres que en mujeres, con 2,5 y 1,6 casos en hombres por cada caso en mujeres en España, respectivamente. En España y Europa, las incidencias del cáncer de pulmón y de colon-recto son las más altas de entre los cánceres en hombres, sólo por detrás del cáncer de próstata. En hombres, las tasas brutas (TB) son más altas en España que en Europa, aunque este gradiente no se mantiene al considerar las tasas estandarizadas por la población mundial (ASR-W).

Los cánceres de mama, pulmón y colon-recto son los tres cánceres más frecuentes en mujeres en España, Europa y el mundo. Las tasas estandarizadas (ASR-W) son muy similares en España y Europa, mientras que en el mundo son más bajas. Sólo en España se diagnostican más de 60.000 casos nuevos cada año de alguno de estos tres cánceres en mujeres.

En la figura 4 se compara la incidencia estandarizada (ASR-W por 100.000 habitantes) estimada para cada localización anatómica y sexo. Para cánceres de colon-recto (en hombres y mujeres) y para cáncer de mama en mujeres, la incidencia es mayor en España que en Europa, que a su vez es mayor que en el mundo. La incidencia del cáncer de pulmón en España se encuentra entre la incidencia europea y mundial tanto en hombres como en mujeres, siendo más cercana a la tasa europea.

Figura 4. Comparación entre la incidencia estandarizada estimada de los cánceres de pulmón, mama y colon-recto en España, Europa y el mundo. ASR-W por 100.000 habitantes.



1.5.2. Mortalidad

En hombres, los cánceres de pulmón y colon-recto son los dos cánceres que provocan más defunciones en España y Europa, con unas 109 muertes por cada 100.000 habitantes en ambos contextos. En mujeres, los cánceres de

mama, pulmón y colon-recto son los tres cánceres más mortales, sumando entre las 3 localizaciones unas 18.000 muertes al año en España, 379.000 en Europa y 1,7 millones en el mundo.

En la tabla 2 se muestra la mortalidad para 2020 observada en España reportada por el Ministerio de Sanidad a partir de los datos del Instituto Nacional de Estadística [24], mientras que para Europa y el Mundo se reportan datos de mortalidad estimados por el ECIS [22] y el GCO [6], respectivamente. Aunque en España hay disponibles datos de mortalidad más recientes (2021), se muestran los datos de 2020 para favorecer la comparación entre regiones.

Tabla 2. Mortalidad observada para España y mortalidad estimada para Europa y el mundo de los cánceres de pulmón, mama y colon-recto por sexo. Número de defunciones, tasa bruta por 100.000 habitantes, tasa estandarizada por la población mundial por 100.000 habitantes y ranking de tipos de cáncer más mortales.

| Sexo | Localización anatómica | Contexto | N | TB | ASR-W | R |
|----------------|------------------------|--------------|-----------|------|-------|----|
| Hombres | Pulmón | España, 2020 | 16.615 | 71,6 | 31,4 | 1º |
| | | Europa, 2020 | 260.019 | 71,9 | 34,9 | 1º |
| | | Mundo, 2020 | 1.188.679 | 30,2 | 25,9 | 1º |
| | Colon-recto | España, 2020 | 8.804 | 37,9 | 14,2 | 2º |
| | | Europa, 2020 | 131.885 | 36,5 | 16,1 | 2º |
| | | Mundo, 2020 | 515.637 | 13,1 | 11,0 | 3º |
| Mujeres | Pulmón | España, 2020 | 5.303 | 22,0 | 9,5 | 3º |
| | | Europa, 2020 | 124.157 | 32,1 | 12,9 | 2º |
| | | Mundo, 2020 | 607.465 | 15,7 | 11,2 | 2º |
| | Mama | España, 2020 | 6.572 | 27,2 | 10,5 | 1º |
| | | Europa, 2020 | 141.765 | 36,6 | 14,8 | 1º |
| | | Mundo, 2020 | 684.996 | 17,7 | 13,6 | 1º |
| | Colon-recto | España, 2020 | 6.170 | 25,6 | 7,4 | 2º |
| | | Europa, 2020 | 112.939 | 29,2 | 9,5 | 3º |
| | | Mundo, 2020 | 419.536 | 10,9 | 7,2 | 3º |

N: Número de defunciones; TB: Tasa bruta por 100.000 habitantes; ASR-W: Tasa

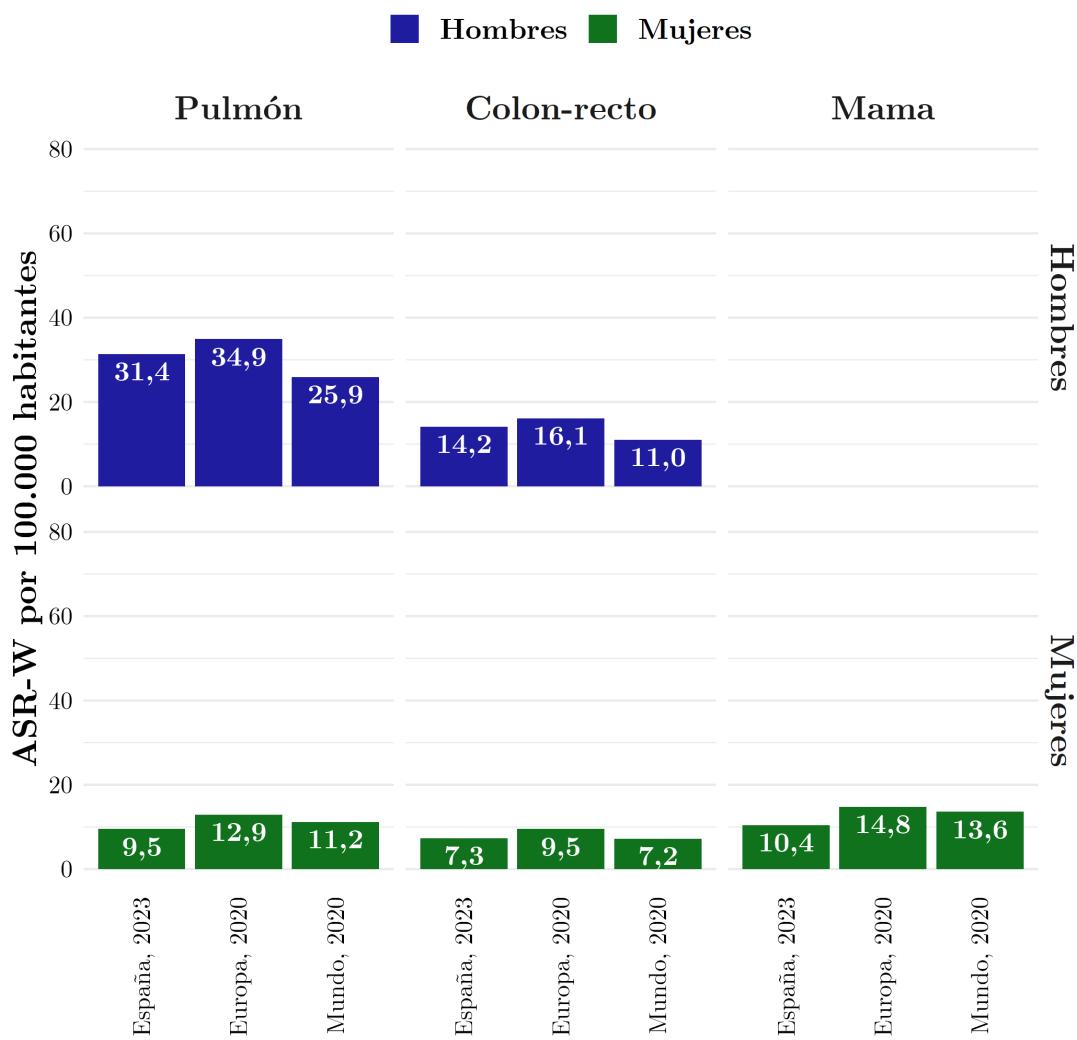
estandarizada por la población mundial por 100.000 habitantes; R: Ranking de tipos de cáncer más mortales.

Los cánceres de pulmón y colon-recto fueron los dos tipos tumorales más mortales en hombres tanto en España como en Europa, provocando más de 1,7 millones de defunciones en el mundo durante el año 2020. En España durante 2020 hubo 72 muertes por cáncer de pulmón y 38 por cáncer de colon-recto por cada 100.000 hombres.

En mujeres españolas, los cánceres más mortales fueron los cánceres de mama, colon-recto y pulmón. El orden cambia ligeramente a nivel europeo y mundial, siendo la mortalidad por cáncer de pulmón más frecuente que por cáncer de colon-recto. De manera combinada, estos tres tipos de cáncer fueron responsables de más de 1,7 millones de defunciones en todo el mundo. En España durante 2020 se produjeron 27 defunciones por cáncer de mama, 26 por cáncer de colon-recto y 22 por cáncer de pulmón por cada 100.000 mujeres.

En la figura 5 se compara la mortalidad estandarizada (ASR-W por 100.000 habitantes) para cada localización anatómica y sexo, usando la misma escala que en la figura 4 para permitir la comparación entre incidencia y mortalidad. En todos los casos, la mortalidad europea es más alta que en España o el mundo.

Figura 5. Comparación entre la mortalidad estandarizada de los cánceres de pulmón, mama y colon-recto en España, Europa y el mundo. ASR-W por 100.000 habitantes.



1.5.3. Supervivencia

Como ocurre en la mayoría de las localizaciones anatómicas, la supervivencia de los cánceres de pulmón, mama y colon-recto ha mejorado considerablemente en las últimas décadas, principalmente debido a importantes avances

terapéuticos y al diagnóstico temprano. Pese a esta mejora, el cáncer de pulmón sigue teniendo uno de los peores pronósticos, tanto en hombres como en mujeres.

En España, los datos de supervivencia más recientes los aporta REDECAN referidos al periodo 2008-2013 con datos de varios RCBP que cubren el 26 % de la población española [45, 46]. En Europa, los resultados de supervivencia más actualizados son los del proyecto EUROCARE-5 [47], mientras que a nivel mundial el estudio CONCORD proporciona datos de 71 países, aunque no llega a estimar resultados globales para la población mundial [48].

En la tabla 3 se compara la supervivencia de los cánceres de pulmón, mama, colon y recto en España y Europa para ambos sexos. Los datos de España corresponden a REDECAN [45, 46] y los de Europa son la media europea del estudio EUROCARE-5 [47], aunque no reporta intervalos de confianza al 95 % para la supervivencia observada.

Tabla 3. Número de casos, supervivencia observada y supervivencia neta a 5 años con intervalo de confianza al 95 % en España (2008-2013) y Europa (2000-2007) de los cánceres de pulmón, mama y colon-recto por sexo.

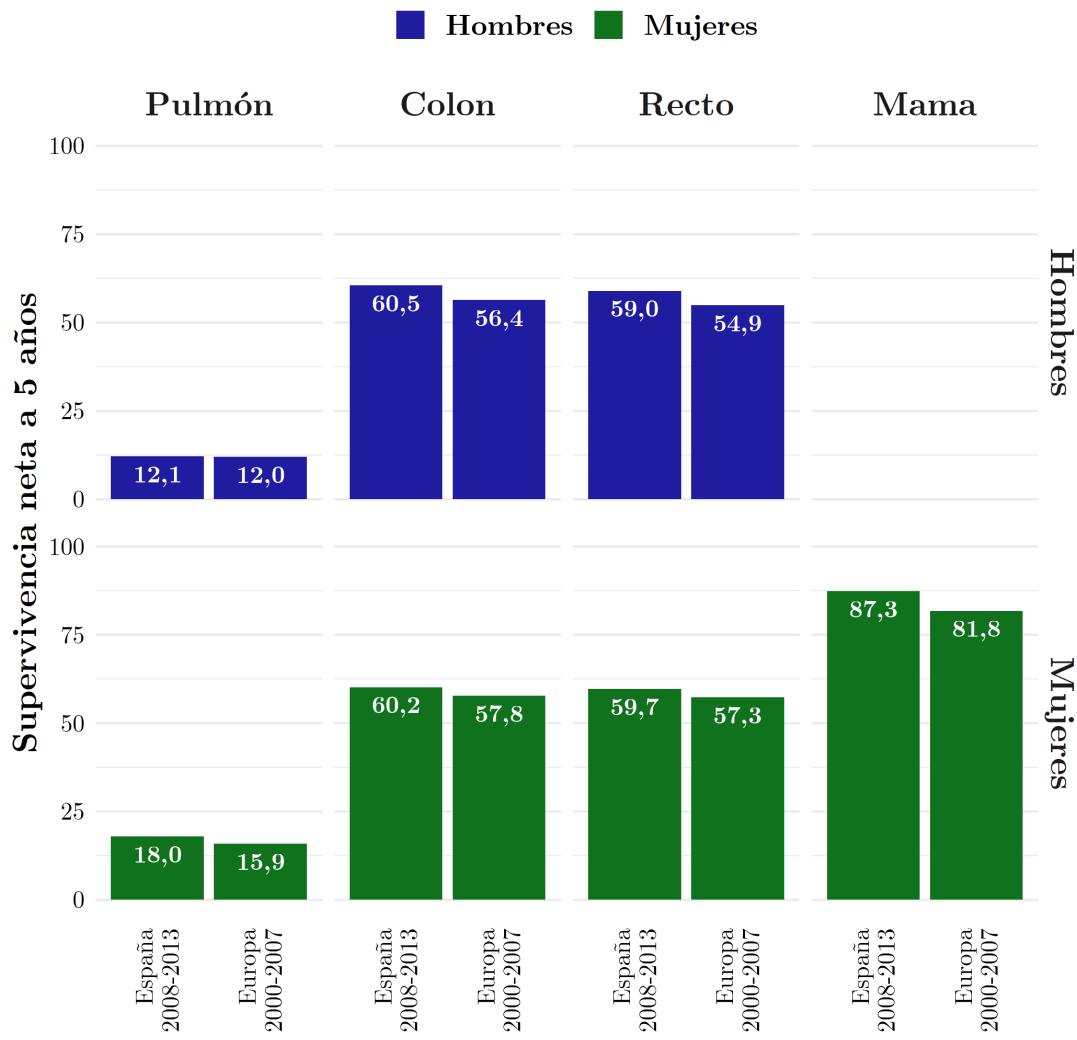
| Sexo | Localización anatómica | Contexto | N | SO 5 años (IC 95 %) | SN 5 años (IC 95 %) |
|----------------|------------------------|----------|---------|---------------------|---------------------|
| Hombres | Pulmón | España | 26.981 | 10,9 (10,5–11,3) | 12,1 (11,6–12,6) |
| | | Europa | 40.406 | 10,5 | 12,0 (11,8–12,1) |
| | Colon | España | 18.121 | 51,2 (50,4–52,0) | 60,5 (59,5–61,5) |
| | | Europa | 98.832 | 47,2 | 56,4 (56,1–56,7) |
| | Recto | España | 9.580 | 51,2 (50,1–52,3) | 59,0 (57,7–60,4) |
| | | Europa | 71.560 | 46,3 | 54,9 (54,5–55,3) |
| Mujeres | Pulmón | España | 6.352 | 17,3 (16,3–18,4) | 18,0 (16,9–19,2) |
| | | Europa | 21.516 | 14,6 | 15,9 (15,6–16,2) |
| | Mama | España | 34.294 | 82,0 (81,6–82,5) | 87,3 (86,8–87,9) |
| | | Europa | 556.376 | 72,5 | 81,8 (81,6–82,0) |
| | Colon | España | 12.488 | 53,3 (52,3–54,2) | 60,2 (59,1–61,3) |
| | | Europa | 96.465 | 51,2 | 57,8 (57,5–58,2) |
| | Recto | España | 5.136 | 53,9 (52,4–55,3) | 59,7 (57,9–61,4) |
| | | Europa | 52.987 | 51,3 | 57,3 (56,8–57,7) |

N: Número de casos; SO: Supervivencia observada a 5 años; SN: Supervivencia neta a 5 años; IC 95 %: Intervalo de confianza al 95 %.

En la figura 6 se compara la supervivencia neta a 5 años en Europa y España para cada localización anatómica y sexo. Se observa que la supervivencia es ligeramente superior en España que en Europa. No obstante, deberíamos considerar dos factores:

- El periodo de diagnóstico de los casos es posterior en España (2008-2013) que en Europa (2000-2007), lo que unido a una continua mejora en los tratamientos y diagnósticos tempranos conlleva una mejor supervivencia.
- La baja supervivencia de algunos cánceres en países de Europa del Este [47].

Figura 6. Comparación entre la supervivencia neta (%) a los 5 años de los cánceres de pulmón, mama, colon y recto en España y Europa.



1.5.4. Prevalencia

En la tabla 4 se muestra la prevalencia estimada para 2020 en España, Europa y el mundo de los cánceres de pulmón, mama y colon-recto. Aunque REDECAN ha publicado estimaciones de prevalencia para España a 31 de diciembre de 2020 [49], para favorecer la comparación se muestran para Es-

paña los datos estimados por el GCO [6] para el mismo año, ya que aporta datos a nivel nacional, europeo y mundial.

El cáncer de mama fue el más prevalente en mujeres seguido por el cáncer de colon-recto, tanto a 1, 3 y 5 años, en el contexto español, europeo y mundial. Esto es debido a su alta incidencia (ver tabla 1) y alta supervivencia (ver tabla 3). En hombres, colon-recto es el cáncer más prevalente por detrás del cáncer de próstata, que cuenta con casi 5 millones (4.956.901) de casos prevalentes en todo el mundo en 2020 [6]. En general, la prevalencia del cáncer de pulmón no es de las más altas en ninguno de los sexos pese a su alta incidencia (ver Tabla 1), dada la alta mortalidad de este cáncer (Tabla 2) y su baja supervivencia (Tabla 3).

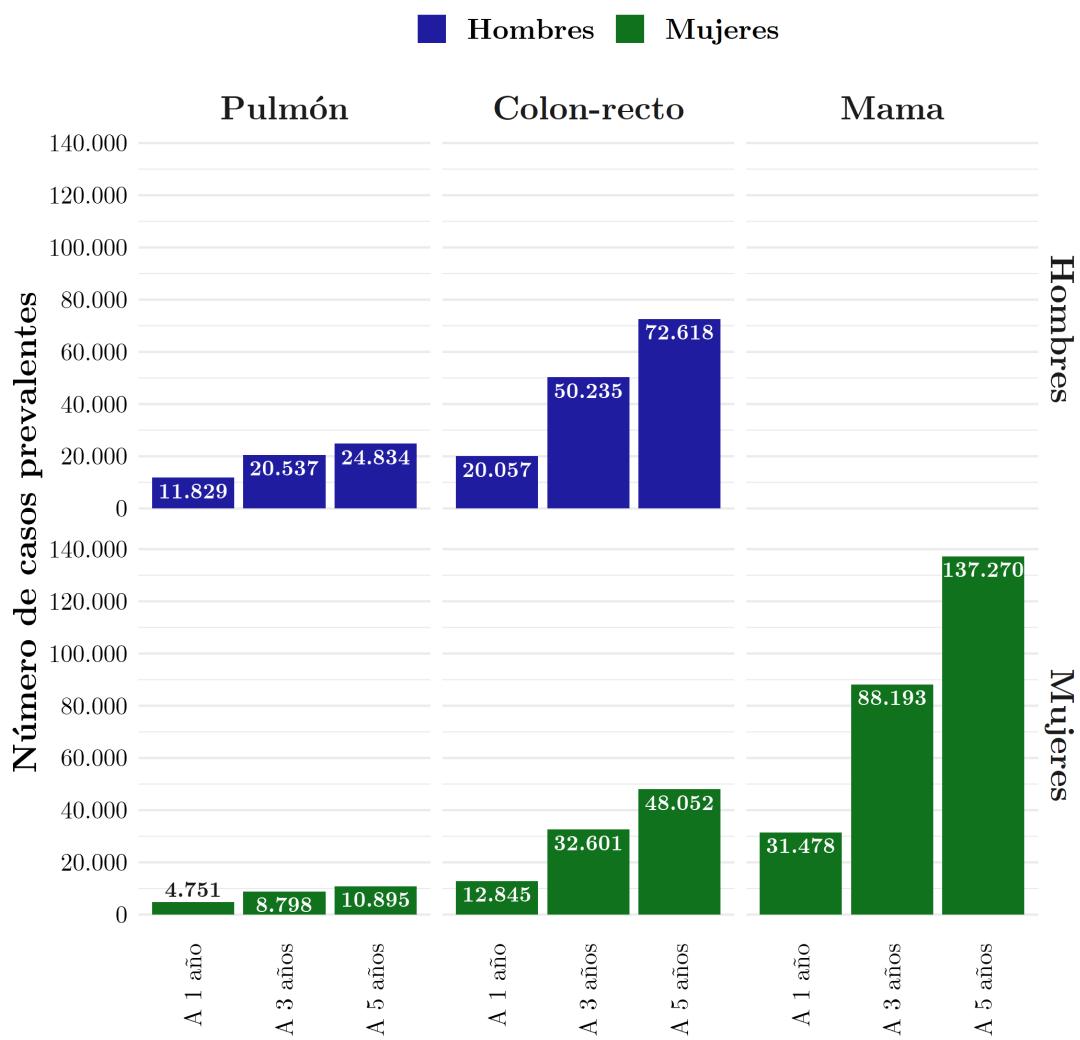
Tabla 4. Prevalencia estimada para 2020 en España, Europa y el mundo de los cánceres de pulmón, mama y colon-recto por sexo. Número de casos prevalentes y ranking de tipos de cáncer más prevalentes a 1, 3 y 5 años.

| Sexo | Localización anatómica | Contexto | 1 año | | 3 años | | 5 años | |
|---------|------------------------|----------|-----------|----|-----------|----|-----------|----|
| | | | N | R | N | R | N | R |
| Hombres | Pulmón | España | 11.829 | 4º | 20.537 | 4º | 24.834 | 4º |
| | | Europa | 169.750 | 3º | 294.998 | 4º | 357.106 | 4º |
| | | Mundo | 734.708 | 3º | 1.290.682 | 3º | 1.579.200 | 3º |
| | Colon-recto | España | 20.057 | 2º | 50.235 | 2º | 72.618 | 2º |
| | | Europa | 227.409 | 2º | 569.621 | 2º | 822.371 | 2º |
| | | Mundo | 800.665 | 2º | 1.990.759 | 2º | 2.850.679 | 2º |
| Mujeres | Pulmón | España | 4.751 | 4º | 8.798 | 5º | 10.895 | 8º |
| | | Europa | 97.789 | 4º | 181.604 | 4º | 225.818 | 6º |
| | | Mundo | 435.811 | 3º | 817.123 | 6º | 1.025.591 | 6º |
| | Mama | España | 31.478 | 1º | 88.193 | 1º | 137.270 | 1º |
| | | Europa | 484.729 | 1º | 1.365.686 | 1º | 2.138.117 | 1º |
| | | Mundo | 1.835.883 | 1º | 5.070.516 | 1º | 7.790.717 | 1º |
| | Colon-recto | España | 12.845 | 2º | 32.601 | 2º | 48.052 | 2º |
| | | Europa | 190.943 | 2º | 484.938 | 2º | 713.797 | 2º |
| | | Mundo | 650.766 | 2º | 1.644.094 | 2º | 2.402.656 | 2º |

N: Número de casos prevalentes; R: Ranking de tipos de cáncer más prevalentes.

En la figura 7 se muestran los casos prevalentes de cáncer de pulmón, mama y colon-recto para España a 1, 3 y 5 años.

Figura 7. Comparación entre la prevalencia de los cánceres de pulmón, mama y colon-recto en España a 1, 3 y 5 años. Número de casos prevalentes.



1.6. Desigualdades socioeconómicas en salud

1.6.1. Nivel socioeconómico y cómo medirlo

El nivel socioeconómico es un factor complejo que puede abarcar varias dimensiones de las circunstancias sociales y económicas de la vida de los individuos y a menudo se mide utilizando información relativa al nivel educativo, nivel de renta o el trabajo de las personas.

Existen principalmente dos enfoques metodológicos para la medición del nivel socioeconómico en entornos científicos. El enfoque individual utiliza información sobre la posición socioeconómica de cada persona (salario, riqueza, tipo de trabajo, educación...), mientras que el enfoque ecológico, o de área, utiliza información agregada como índices de privación socioeconómica que consideran factores demográficos, sociales y económicos de la zona de residencia [50]. Si bien ambos enfoques ofrecen información útil y complementaria, la magnitud y el tipo de desigualdades identificadas pueden variar mucho de un planteamiento a otro. Cada indicador tiene ventajas y desventajas específicas [51] y es importante tener en cuenta los sesgos que se pueden cometer al intentar medir el nivel socioeconómico. Por ejemplo:

- La edad es un factor con gran influencia en el salario individual [51], que se suele incrementar conforme aumenta la edad.
- Medir el nivel socioeconómico usando el tipo de trabajo puede ser problemático para determinados grupos de población como personas jubiladas, adolescentes o embarazadas [52, 53].
- La educación recogida suele capturar únicamente aquella formación reglada, dejando a un lado otros tipos de formación como la vocacional o la recibida durante el trabajo [51].
- Los índices agregados no siempre reflejan con exactitud las medidas individuales. Además, en la interpretación de resultados es fácil caer en la falacia ecológica.

Si bien en algunas partes de Europa existe una larga tradición de medir la privación socioeconómica en áreas pequeñas [54–56], no es este el caso de España. Por contextualizar este hecho, en el año 2016 se publicó un índice de privación a nivel de sección censal para España que estaba referido al año 2001 [57]. Otros proyectos de investigación como MEDEA [58, 59] han desarrollado índices de privación para ciudades específicas, pero no a nivel nacional. Más recientemente, en 2021, se publicó un índice de privación referido al año 2011 a nivel de sección censal que cubre toda España [60]. Esta tesis doctoral mide el nivel socioeconómico utilizando ese índice de privación, que será comentado con más detalle en la sección de metodología. La necesidad de un índice de estas características se ha traducido en que este artículo se ha convertido en el más citado de la revista Gaceta Sanitaria durante el año 2022 [61].

1.6.2. Desigualdades socioeconómicas en cáncer

Se ha constatado que factores como la posición socioeconómica, la raza, la etnia y el lugar de residencia producen importantes desigualdades en diversos resultados relacionados con el cáncer [8, 50, 62–64].

Reducir las desigualdades en materia de cáncer es uno de los principales objetivos del Plan Europeo de Lucha Contra el Cáncer de la Comisión Europea [65], entendiendo como desigualdades toda diferencia en cáncer por cuestión de género, discapacidad, colectivos desfavorecidos y marginados, etnia y pobreza. En la comunicación de la Comisión al Parlamento Europeo y al Consejo, se afirma que “(las) desigualdades son inaceptables en una Unión Europea de la Salud que pretende proteger a todos. En la Unión no debería haber pacientes con cáncer de primera y segunda clase”. Dentro de esta iniciativa, se ha creado el Registro Europeo de Desigualdades en Cáncer, que busca determinar las desigualdades existentes en cáncer y plantear acciones para reducirlas, tanto entre países de la Unión Europea como dentro de ellos [66].

En el Registro Europeo de Desigualdades en Cáncer, la Comisión Europea

ha creado perfiles específicos para cada país de la Unión Europea [66]. En el caso de España, centrándonos en las desigualdades socioeconómicas [67], este informe destaca que:

- La proporción de fumadores diarios de cigarrillos es alta en España, con importantes desigualdades socioeconómicas:
 - Uno de cada cinco adultos fumó cigarrillos diariamente durante 2019, siendo el hábito tabáquico diario mayor en hombres (23 % vs. 16 % en mujeres) y en adultos no ancianos (23 % en menores de 65 años vs. 8 % en personas de 65 años o más).
 - En 2019, la proporción de fumadores diarios adultos era casi un tercio mayor entre las personas con menor nivel educativo (21 %) que entre las personas con mayor nivel educativo (16 %).
 - La proporción de fumadores diarios entre personas con bajos ingresos era aproximadamente el 25 %, mientras que entre los que se encontraban en el extremo más alto de la distribución de ingresos la prevalencia de fumadores era del 14 %, con esta brecha ampliándose desde el año 2014.
- Pese a la alta adherencia al programa de cribado de cáncer de mama, existen grandes desigualdades socioeconómicas. En 2019, el 74 % de las mujeres en edad de cribado (50-69 años) se realizó una mamografía en los últimos 2 años, pero hubo importantes diferencias en la participación en el cribado en función del nivel educativo (71 % en el nivel educativo más bajo vs. 77 % en el más alto) y del nivel de ingresos (67 % en el nivel de ingresos más bajo vs. 79 % en el más alto).
- La evaluación de las desigualdades socioeconómicas en la participación y resultados de los programas de cribado aún no están totalmente implementadas a pesar de los esfuerzos realizados en nuestro país: en 2020 el 90 % de las comunidades autónomas españolas monitorizan estas desigualdades para los programas de cribado del cáncer de mama, pero este porcentaje disminuye para los cribados de cáncer de colon-recto (80 %) y de cuello uterino (50 %) [68].

En definitiva, es un hecho que el impacto del cáncer en la población está aumentando, estimándose en 30 millones los casos nuevos de cáncer en todo el mundo en 2030 [69], lo que ejerce una presión significativa sobre las poblaciones, en general, y sus sistemas sanitarios, en particular. Además, dado el cambio sociodemográfico de las sociedades occidentales, asociado al envejecimiento, el papel de la edad en el riesgo de cáncer y los avances tecnológicos en el diagnóstico y tratamiento del cáncer, no siempre justificados, la vigilancia y el control de esta enfermedad se está convirtiendo en uno de los retos sanitarios más complejos del futuro inmediato [70]. A pesar de los esfuerzos políticos realizados a nivel mundial y europeo, las desigualdades sociales y su impacto en el cáncer son un problema persistente [71], tanto en lo referente a la igualdad de oportunidades en todas las etapas de la historia natural de enfermedad, como en el alto impacto económico sobre los costes sanitarios, tanto directos como indirectos [72]. Por lo tanto, identificar y caracterizar las desigualdades socioeconómicas en los resultados del cáncer podría ayudar a optimizar y redistribuir los servicios sanitarios de una forma más equitativa.

1.7. Justificación

En primer lugar, el cáncer es un grave problema de salud pública dada su magnitud, trascendencia y potencial vulnerabilidad. En concreto, los cánceres de pulmón, mama y colon-recto son los cánceres más frecuentes y son tumores muy diferentes en cuanto a su prevención y pronóstico.

Desafortunadamente, la disponibilidad de indicadores epidemiológicos de estos cánceres por nivel socioeconómico es muy escasa en nuestro país. Dada la importancia descrita anteriormente de las desigualdades socioeconómicas en cáncer, disponer de estos indicadores sería relevante a la hora de desarrollar políticas de salud pública enfocadas a reducir estas desigualdades en las posibilidades de la prevención de la enfermedad, el diagnóstico y el tratamiento.

Por otro lado, en la evidencia científica disponible se ha detectado la ausencia de síntesis sobre el impacto del nivel socioeconómico en el cáncer. A nivel

nacional también existen importantes lagunas de tal forma que se desconoce cómo los principales indicadores epidemiológicos del cáncer varían según el nivel socioeconómico. Los pocos estudios sobre incidencia y mortalidad de cáncer disponibles en España se limitan a algunas provincias o grandes ciudades, no constituyendo una muestra representativa de la realidad nacional. Y si nos centramos en supervivencia, la principal causa de que en España no esté reportada la supervivencia neta de cáncer por nivel socioeconómico es la ausencia de herramientas para su cálculo. Es decir, no existen tablas de vida por nivel socioeconómico, algo que limita los tipos de análisis de supervivencia que se pueden realizar a nivel poblacional.

Por lo tanto, resulta necesario llevar a cabo una investigación explorando el impacto de las desigualdades socioeconómicas en los principales indicadores epidemiológicos del cáncer en España.

Objetivos

2.1. Objetivo principal

Conocer el impacto del nivel socioeconómico en los principales indicadores epidemiológicos del cáncer en España.

2.2. Objetivos específicos

1. Conocer el impacto del nivel socioeconómico en los resultados del cáncer de pulmón.
2. Conocer el impacto del nivel socioeconómico en la esperanza de vida en España y generar las primeras tablas de vida por nivel socioeconómico para España.
3. Conocer el impacto del nivel socioeconómico en la incidencia de los cánceres de pulmón, mama y colon-recto.
4. Conocer el impacto del nivel socioeconómico en la mortalidad por cáncer de pulmón en España.

Para responder a cada objetivo específico se ha elaborado y publicado un artículo científico en revistas indexadas en el *Journal Citation Reports* (JCR).

Metodología

En esta sección se muestra un resumen de la metodología utilizada para responder a cada uno de los objetivos específicos enunciados anteriormente:

1. Conocer el impacto del nivel socioeconómico en los resultados del cáncer de pulmón.
2. Conocer el impacto del nivel socioeconómico en la esperanza de vida en España y generar las primeras tablas de vida por nivel socioeconómico para España.
3. Conocer el impacto del nivel socioeconómico en la incidencia de los cánceres de pulmón, mama y colon-recto.
4. Conocer el impacto del nivel socioeconómico en la mortalidad por cáncer de pulmón en España.

Una descripción más detallada de los métodos se puede encontrar en el apartado de métodos de las publicaciones científicas asociadas a la tesis doctoral (página 123).

3.1. Metodología del objetivo específico 1

Para responder al primer objetivo específico se diseñó una umbrella review: una revisión de revisiones sistemáticas.

El protocolo de investigación se registró en PROSPERO (*International Prospective Register of Systematic Reviews*) con ID CRD42021282194 [73].

Los principales criterios de inclusión para la umbrella review fueron los siguientes:

- Población: Revisiones sistemáticas que tuviesen por objeto pacientes adultos (≥ 18 años) diagnosticados de cáncer de pulmón.
- Exposición: Nivel socioeconómico. Se consideraron las revisiones sistemáticas en las que se comparaban resultados entre pacientes de nivel socioeconómico relativamente bajo y alto, incluyendo medidas tanto individuales como de área.
- Resultado: Indicadores epidemiológicos de cáncer de pulmón (incidencia, mortalidad, supervivencia, prevalencia) y otros indicadores relacionados con el cáncer de pulmón como el cribado, métodos diagnósticos o tratamientos.
- Diseño de las revisiones: Se consideraron revisiones sistemáticas que reportan la relación entre nivel socioeconómico y cualquiera de los resultados de cáncer de pulmón antes enunciados.
- Criterios de exclusión:
 - Artículos publicados en 2009 o antes, con el objetivo de excluir revisiones que no incluían la evidencia científica más reciente.
 - Revisiones que se centraban en otros tipos de desigualdades (por ejemplo, por género, raza, área rural vs área urbana, etc.).
 - Revisiones que no informaban de resultados específicos de cáncer de pulmón.
 - Revisiones que informaban sobre la prevalencia del tabaquismo, otros factores de riesgo u otros resultados no directamente relacionados con la magnitud, el diagnóstico o tratamiento del cáncer de pulmón.
 - Revisiones que estaban en un idioma diferente al inglés, español, alemán, holandés, portugués, ruso o búlgaro, o cuyo texto com-

pleto no se pudo obtener después de contactar con el autor de referencia.

- Aquellas revisiones que no se consideraron sistemáticas en base a la definición de Martinic et al. [74].
- Estrategia de búsqueda: Se realizaron búsquedas en Medline a través de PubMed, Scopus y Web of Science desde el 1 de enero de 2010 hasta el 26 de octubre de 2021. También se realizó una búsqueda manual en Google Scholar para tesis, pre-prints y otros trabajos no publicados. No hubo restricciones por idioma en la búsqueda y se identificaron estudios adicionales que se consideraron relevantes al revisar las referencias de los trabajos encontrados. La estrategia completa de búsqueda está disponible en *Open Science Framework* [75].
- Selección de artículos: Se utilizó el software Covidence para gestionar todas las etapas de la revisión. Los artículos se filtraron en base a su título, abstract y texto completo por dos revisores, resolviendo los desacuerdos mediante discusión. Un investigador extrajo los datos de los artículos, que posteriormente fueron revisados por un segundo investigador.
- Calidad de las revisiones sistemáticas: Se evaluó el riesgo de sesgos usando la herramienta AMSTAR-2 [76] de forma independiente por dos investigadores. AMSTAR-2 consiste en 16 ítems que evalúan el rigor de revisiones sistemáticas de estudios no aleatorizados [76], de los cuales 5 ítems fueron considerados como críticos dado el contexto. Las revisiones sistemáticas fueron evaluadas con confianza “alta” (buenos estudios con bajo riesgo de sesgos), “moderada” (riesgo medio de sesgos) o “baja” (alto riesgo de sesgos). La falta de acuerdo en cualquier ítem de AMSTAR-2 fue revisada y resuelta por discusión entre los investigadores.
- Síntesis de datos: Los datos se sintetizaron de forma narrativa, considerando la cantidad de evidencia disponible y el riesgo de sesgos de cada revisión sistemática.

3.2. Metodología del objetivo específico 2

Datos y diseño del estudio

Se planteó un estudio multinivel de base poblacional. Se extrajeron datos de población y mortalidad general para España durante el periodo 2011-2013 por sección censal, grupo de edad, año y sexo del Instituto Nacional de Estadística (INE).

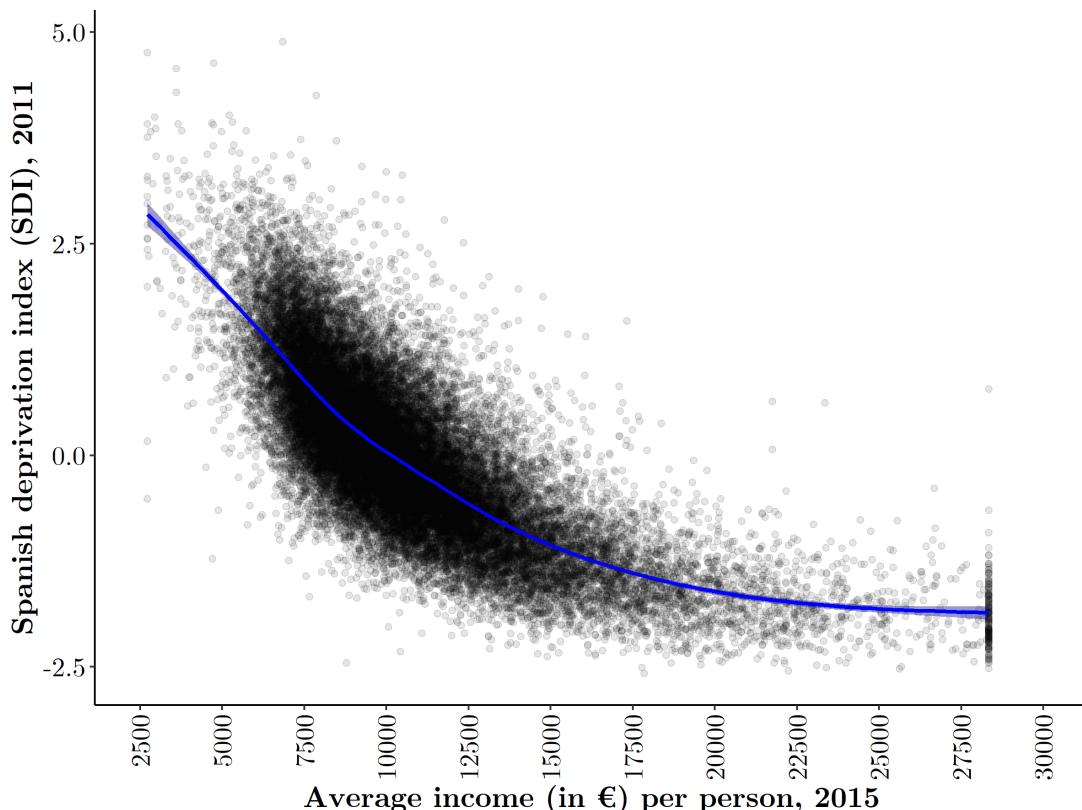
Para medir el nivel socioeconómico, se utilizó el índice de privación creado por Duque et al. [60] a nivel de sección censal para España. Este índice está referido al año 2011 y se construyó utilizando los datos del Censo de Población y Viviendas realizado en 2011 por el INE. El índice de privación está basado en los siguientes seis indicadores:

- Población trabajadora manual.
- Población asalariada eventual.
- Desempleo.
- Personas de 16 y más años con instrucción insuficiente.
- Personas de 16 a 29 años con instrucción insuficiente.
- Viviendas principales sin acceso a Internet.

En este estudio, se dividió el índice de privación de Duque et al. [60] en quintiles (Q), donde Q5 representa las zonas de nivel socioeconómico más bajo (mayor privación) y Q1 el 20 % de las áreas de nivel socioeconómico más alto (menor privación).

Pese a que este índice no cuenta con información directa sobre salario, en un análisis de sensibilidad se encontró una asociación directa entre el índice de privación y el salario medio por persona a nivel de sección censal (Figura 8).

Figura 8. Relación entre salario medio por persona en 2015 e índice de privación de Duque et al. con suavizado GAM (generalised additive model).



Fuente: Figura Suplementaria 2 del trabajo 3. Elaboración propia.

Análisis estadístico

Se calcularon las tasas brutas de mortalidad general por quintil de privación, grupo de edad y sexo en España. Se generó un modelo para cada sexo, modelizando el número de muertes siguiendo un modelo lineal generalizado (GLM) que considera un error de Poisson y depende del efecto suavizado de la edad y del quintil de privación, teniendo en cuenta la población a riesgo como un offset.

Del modelo se deriva la esperanza de vida para todos los grupos de edad, teniendo especial interés la esperanza de vida al nacimiento. Mediante medias ponderadas por población, se calculó la esperanza de vida al nacimiento

para cada provincia.

El código desarrollado para el análisis y las tablas de vida generadas por provincias están disponibles de forma abierta en GitHub [77]. Para la gestión de datos y el análisis estadístico se usó Stata v.16.1 [78] y R v.4.1.0 [79].

3.3. Metodología del objetivo específico 3

Datos y diseño del estudio

En relación con el tercer objetivo, se desarrolló un estudio multinivel de base poblacional.

Los datos de incidencia de cáncer de pulmón, mama en mujeres y colon-recto proceden de 9 RBCP provinciales (Albacete, Bizkaia, Castellón, Cuenca, Girona, Gipuzkoa, Granada, Navarra y Tarragona) que participaron en los Estudios Europeos de Alta Resolución [80]. En la Figura 9 se muestran las provincias que aportaron datos para cada localización anatómica: 7 provincias aportaron datos de cáncer de colon-recto, 2 de cáncer de pulmón y 6 de cáncer de mama en mujeres.

Figura 9. Mapa de España peninsular con las provincias que aportaron datos por localizaciones (A: colon-recto, B: pulmón, C: mama en mujeres).



Los casos nuevos de cáncer fueron diagnosticados en personas >18 años durante el periodo 2010-2013. Para la identificación de los casos, se utilizó la Clasificación Internacional de Enfermedades Oncológicas, 3^a edición [81]. Los códigos usados para cada localización anatómica fueron: C18-C21 para colon-recto, C34.0-C34.9 para cáncer de pulmón y C50.0-C50.9 para cáncer de mama en mujeres.

Las direcciones postales de residencia de cada paciente de cáncer en el momento del diagnóstico fueron geocodificadas usando la aplicación GEO_CIBER. La geocodificación se realizó de forma automática cuando fue posible y manualmente en aquellos casos donde la coincidencia automática de una dirección con sus coordenadas encontradas por GEO_CIBER era baja y por tanto susceptible de ser errónea. Tras la geocodificación de cada dirección, se obtuvo la sección censal de residencia al diagnóstico de cada caso de cáncer, usando para ello la capa de secciones censales del Censo de 2011 realizado por el INE.

Los datos de población por sexo, año, edad y sección censal se obtuvieron del INE.

Al igual que en la metodología del objetivo específico 2, para medir el nivel socioeconómico se utilizó el índice de privación desarrollado por Duque et al. [60], detallado a nivel de sección censal y referido al año 2011, dividido en quintiles.

Análisis estadístico

En un primer enfoque descriptivo para todo el periodo, se calcularon las tasas brutas por cada 100.000 personas por quintiles de privación, grupos de edad y sexo. Posteriormente, se calcularon ratios de tasas ajustadas univariadas y multivariadas utilizando un modelo de Poisson de efectos mixtos [82] estratificado por sexo. Se fueron realizando modelos adicionales agregando una variable en cada paso para controlar la confusión.

A partir de los modelos, se derivó la estimación bayesiana empírica para identificar patrones de variación no aleatoria [83] en la incidencia de los cánceres de colon-recto, pulmón y mama en España. Se realizaron mapas con las tasas de incidencia suavizadas ajustadas por edad e índice de privación por sección censal para los distintos cánceres.

Para la gestión de datos y el análisis estadístico se usaron Stata v.16 [78] y R v.4.0.2 [79].

3.4. Metodología del objetivo específico 4

Datos y diseño del estudio

La información de mortalidad por cáncer de pulmón se obtuvo del INE, tras una solicitud de acceso a datos confidenciales (expediente BE099-2021). Se consideraron todas las defunciones por cáncer de pulmón (C33-34 en la Clasificación Internacional de Enfermedades, 10^a edición [84]) en España durante el periodo 2011-2017, desagregadas por sección censal de residencia en el momento del fallecimiento, año, edad y sexo.

Al igual que en la metodología de los objetivos específicos 2 y 3, para medir el nivel socioeconómico se utilizó el índice de privación desarrollado por Duque et al. [60], detallado a nivel de sección censal y referido al año 2011, dividido en quintiles.

Análisis estadístico

Se calculó el número esperado de muertes por cáncer de pulmón para cada sección censal y sexo, para calcular después las razones suavizadas estandarizadas de mortalidad, usando un modelo condicional autoregresivo [85]. Para el suavizado, se utilizaron las vecindades de cada sección censal. Los modelos se ajustaron usando INLA (*Integrated Nested Laplace Approximation*)

tions for Bayesian inference) con el paquete R-INLA [86, 87].

Se calcularon las tasas brutas y estandarizadas por edad por la población europea (ASR-E) para cada quintil de privación, sexo y año, utilizando la población estándar europea de 2013 [34]. Para comparar la mortalidad entre los niveles socioeconómicos se calcularon las razones de ASR-E (Q5 vs. Q1), obtenidos tras dividir la ASR-E de Q5 (nivel socioeconómico más bajo) entre la ASR-E de Q1 (nivel socioeconómico más alto).

Se usó R v.4.2.0 [79] para la gestión de datos, análisis estadístico y creación de mapas. Los paquetes ggplot2 v.3.4.0 [88] y sf v.1.0-9 [89] se usaron para generar las figuras.

3.5. Aspectos éticos

Los dos proyectos de investigación en los que se basa esta tesis doctoral han recibido la aprobación del Comité de Ética de la Investigación Biomédica de Granada (estudio 0072-N-18). Se respetaron los principios éticos recogidos por la Declaración de Helsinki [90].

Las entidades financieradoras no tuvieron ningún papel en el diseño del estudio, en la recopilación, análisis e interpretación de los datos, en la redacción de los artículos ni en la decisión de publicar los resultados.

Los datos de mortalidad por cáncer de pulmón a nivel de sección censal son confidenciales debido al grado de desagregación que presentan. Para su obtención, se cursó una solicitud al INE de acceso a microdatos confidenciales con fines científicos, resuelta favorablemente con expediente BE099-2021.

Resultados

En esta sección se resumen los resultados obtenidos para cada uno de los objetivos específicos:

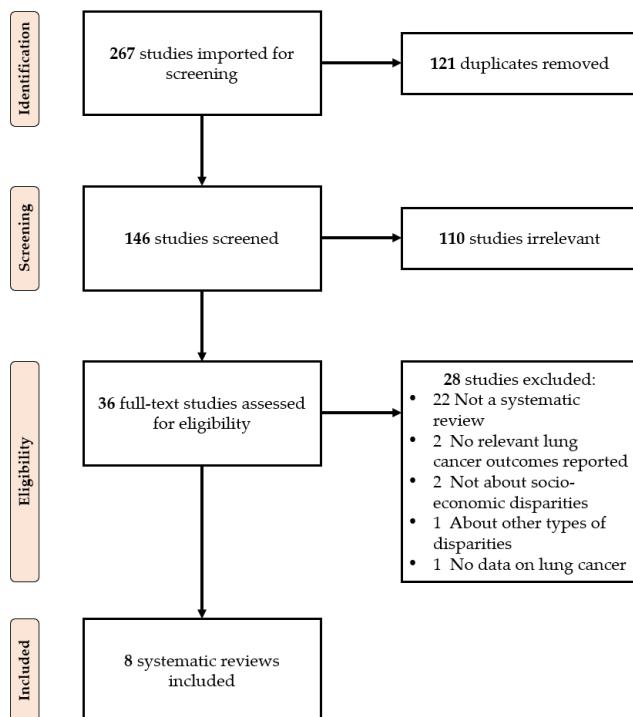
1. Conocer el impacto del nivel socioeconómico en los resultados del cáncer de pulmón (artículo 1).
2. Conocer el impacto del nivel socioeconómico en la esperanza de vida en España y generar las primeras tablas de vida por nivel socioeconómico para España (artículo 2).
3. Conocer el impacto del nivel socioeconómico en la incidencia de los cánceres de pulmón, mama y colon-recto (artículo 3).
4. Conocer el impacto del nivel socioeconómico en la mortalidad por cáncer de pulmón en España (artículo 4).

Una descripción más detallada de los resultados se puede encontrar en el apartado de las publicaciones asociadas a la tesis doctoral (página 123).

4.1. Resultados del objetivo específico 1

En la figura 10 se muestra el diagrama de flujo de la selección de revisiones sistemáticas. Se incluyeron 8 de los 267 estudios identificados inicialmente.

Figura 10. Diagrama de flujo del proceso de selección de revisiones.



Del total de estudios identificados, 121 revisiones sistemáticas se eliminaron por ser duplicados, 110 tras el cribado por título, abstract y texto completo cuando fue necesario, y 28 en una fase final considerando todos los criterios de exclusión. La principal razón de exclusión de cada estudio considerado, de manera individual, se puede encontrar en *Open Science Framework* [75].

Estas 8 revisiones sistemáticas analizaban 220 estudios originales que examinaban 8 tipos distintos de resultados en cáncer de pulmón: mortalidad, supervivencia, uso de cribado, duración de intervalos de cuidados, presentación de urgencias, estadio al diagnóstico, uso de métodos diagnósticos y tratamientos. Casi todos los estudios originales provenían de países con altos ingresos (Estados Unidos, Reino Unido, Unión Europea y Australia).

En el artículo completo (página 123) se muestran tablas con las principales características y resultados de cada revisión sistemática incluida en el

estudio: cómo midieron el nivel socioeconómico, qué periodo de búsqueda tenía cada estudio, número de estudios originales incluidos, representación geográfica de los estudios, número de participantes, principales resultados, variables de ajuste de los análisis, instrumento utilizado para medir la calidad metodológica de los estudios originales, resumen de la calidad metodológica y principales limitaciones de cada revisión.

En relación con la calidad metodológica, 4 revisiones fueron clasificadas como revisiones de “confianza moderada” y otras 4 como revisiones de “confianza baja” (Figura 11).

Figura 11. Riesgo de sesgos para las revisiones sistemáticas usando los ítems de la herramienta AMSTAR-2.

| First author, publication year | AMSTAR-2 items | | | | | | | | | | | | | | | | Confidence in results | | | | | | | | | | | | | | |
|--------------------------------|-------------------|------------|---|----------------------------|----|---------------------|---|-----------------|----|-----------------|----|------------------|----|------------------------|----|---------------------------|-----------------------|-----------------------------|----|-----------------------|----------|---------------------------------|---|-------------------------------|---|---------------|---|------------------|---|----------------------|--|
| | Research question | * Protocol | | Selection of study designs | | * Literature search | | Study selection | | Data extraction | | Excluded studies | | Description of studies | | * Risk of bias assessment | | Funding of original studies | | * Statistical methods | | Impact of risk of bias analysis | | * Risk of bias interpretation | | Heterogeneity | | Publication bias | | Conflict of interest | |
| | | Y | Y | N | PY | N | Y | N | Y | Y | Y | N | NA | NA | Y | Y | Y | Y | Y | Y | NA | Y | Y | Y | Y | Y | Y | Y | Y | Y | |
| Afshar, 2021 | Y | Y | N | PY | N | Y | N | Y | Y | Y | N | NA | NA | Y | Y | NA | Y | Y | Y | NA | Y | Moderate | | | | | | | | | |
| Finke, 2018 | Y | Y | N | PY | N | Y | N | Y | Y | PY | N | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Moderate | | | | | | | | | |
| Forrest, 2013 | Y | PY | N | PY | Y | Y | N | Y | PY | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Y | Moderate | | | | | | | | | |
| Forrest, 2017 | Y | Y | N | PY | Y | N | N | PY | PY | N | Y | Y | Y | Y | Y | Y | Y | Y | N | Y | Moderate | | | | | | | | | | |
| Mitchell, 2015 | Y | N | N | PY | Y | N | N | Y | N | N | NA | NA | Y | Y | NA | NA | Y | Y | NA | Y | Y | Low | | | | | | | | | |
| Norris, 2020 | Y | Y | N | PY | N | Y | N | Y | PY | N | N | N | N | N | N | N | Y | Y | Y | Y | Y | Low | | | | | | | | | |
| Sosa, 2021 | Y | N | Y | PY | Y | Y | N | PY | PY | N | NA | NA | N | N | N | N | NA | NA | N | N | Y | Low | | | | | | | | | |
| Wang, 2020 | Y | N | N | PY | N | Y | N | PY | PY | N | Y | N | N | N | N | N | N | N | N | Y | Y | Low | | | | | | | | | |

N: No; NA: Not available because no meta-analysis was done; PY: Partial Yes; Y: Yes

* Critical item of AMSTAR-2

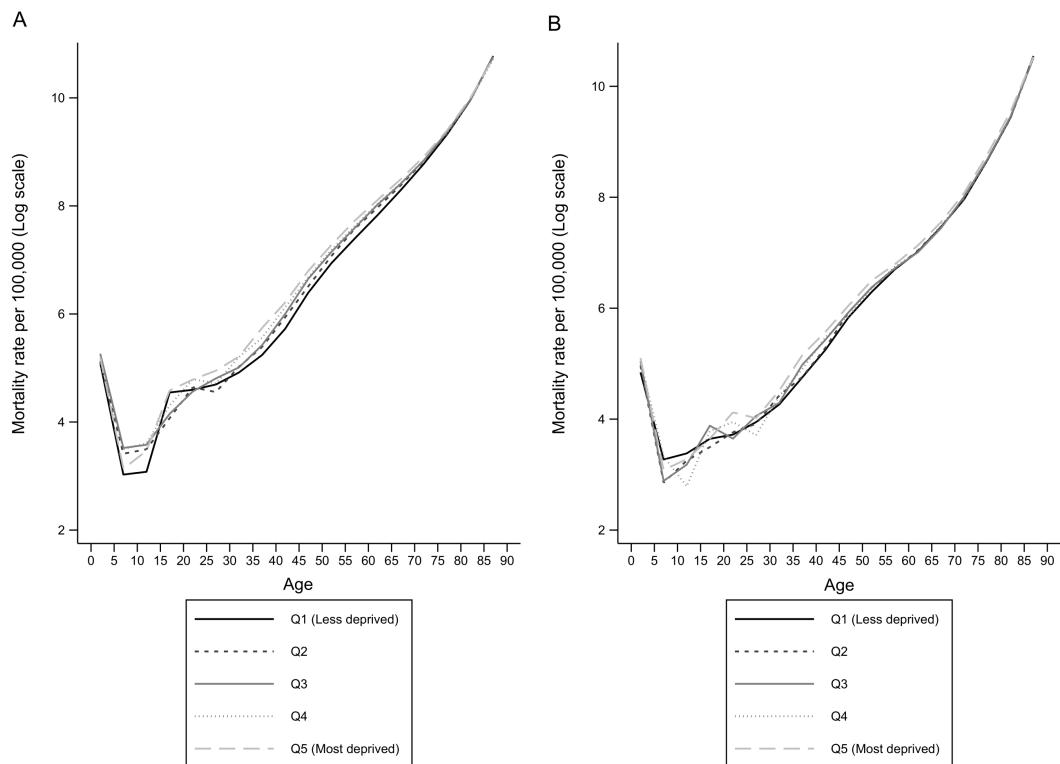
Los principales resultados de la umbrella review se pueden agrupar según el resultado que consideran de cáncer de pulmón:

- Incidencia: no se encontró ninguna revisión sistemática relacionada con la incidencia de cáncer de pulmón que cumpliese los criterios de inclusión.
- Mortalidad: Wang et al. [91] encontraron que un nivel socioeconómico en la infancia más bajo se relacionó con una mayor mortalidad por cáncer de pulmón.
- Cribado: Sosa et al. [92] hallan relevantes desigualdades socioeconómicas en el cribado en Estados Unidos a favor de las clases altas.
- Duración de los intervalos de cuidados: Forrest et al. [93] no encontraron diferencias en la duración de diferentes intervalos de cuidados por nivel socioeconómico.
- Urgencias: Forrest et al. [93] y Mitchell et al. [94] hallan que los pacientes de cáncer de pulmón de un nivel socioeconómico más bajo tienen más probabilidades de acudir a los servicios de urgencias.
- Estadio al diagnóstico: en el meta-análisis realizado por Forrest et al. [93] no encontraron desigualdades socioeconómicas en el estadio al diagnóstico del cáncer de pulmón.
- Tratamiento: Forrest et al. [95] y Norris et al. [96] demuestran que los pacientes de cáncer de pulmón de bajo nivel socioeconómico tienen menos probabilidades de recibir determinados tratamientos tanto convencionales (cirugía y quimioterapia) como propios de la medicina de precisión.
- Supervivencia: Finke et al. [97] encontraron asociación entre una peor supervivencia y bajos salarios, bajo nivel educativo y bajo nivel socioeconómico. Afshar et al. [63] concluyen que las desigualdades existentes pueden deberse al tipo de tratamiento recibido y a la presencia de comorbilidades.

4.2. Resultados del objetivo específico 2

Durante el periodo 2011-2013, la mortalidad general fue mayor en hombres que en mujeres. Las zonas con nivel socioeconómico más bajo tuvieron mayor mortalidad general que las zonas de nivel socioeconómico más alto (un 17-20 % mayor para hombres y un 6-10 % para mujeres). La mortalidad por grupos de edad representada en escala logarítmica tiene forma de U tanto en hombres como en mujeres (Figura 12), con una mayor tasa de defunciones en los grupos extremos de edad.

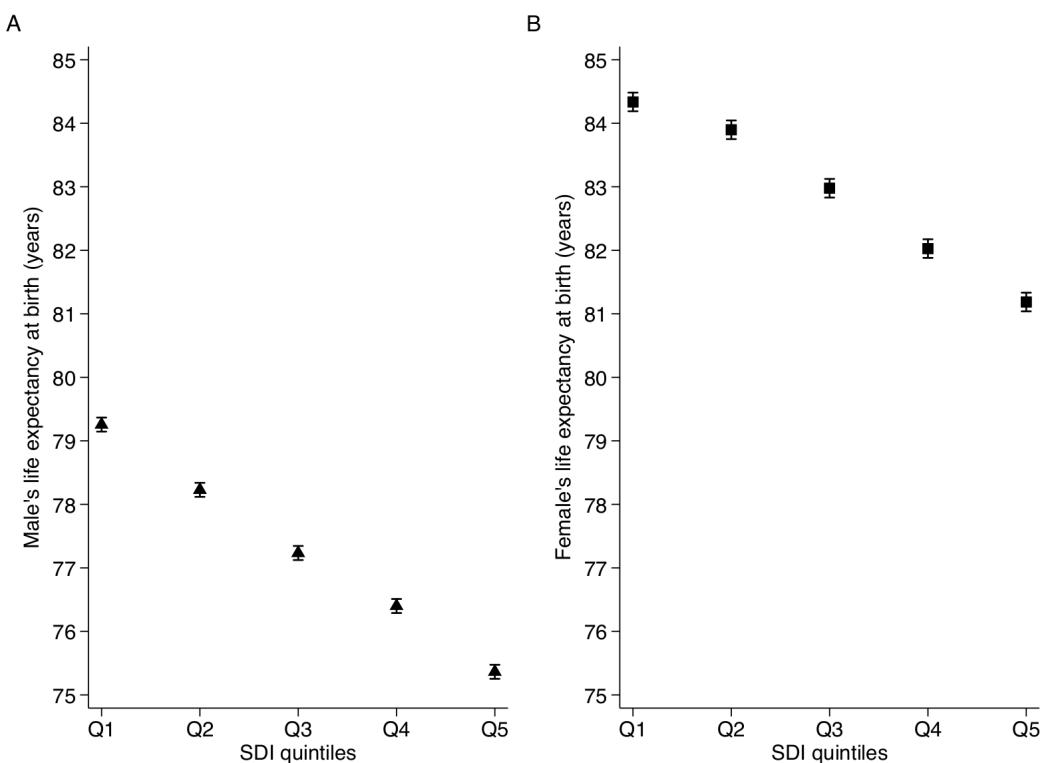
Figura 12. Tasas observadas de mortalidad por 100.000 personas por sexo (A: hombres, B: mujeres), quintil de privación y grupo de edad en España, 2011-2013. Escala logarítmica.



fue de 77,3 años en hombres y 82,9 años en mujeres.

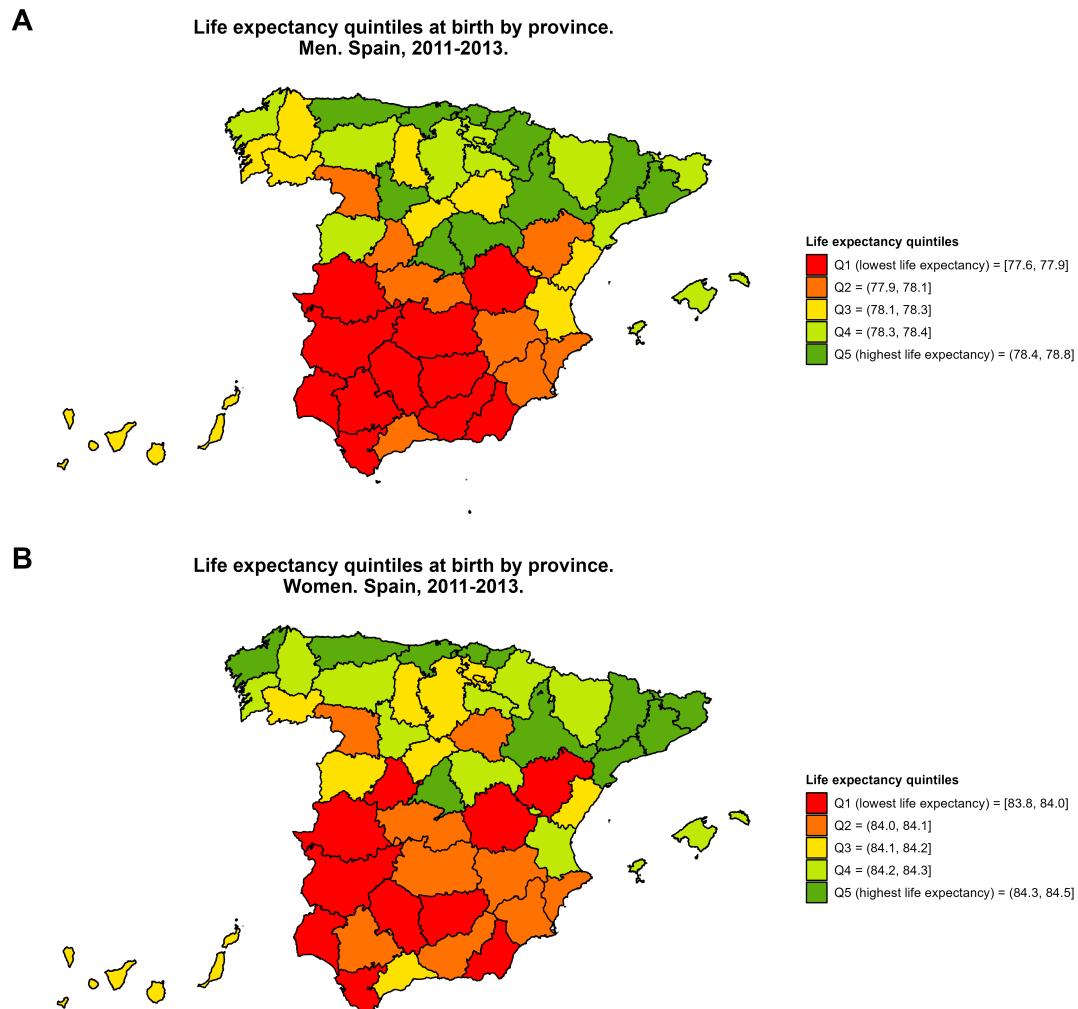
Existe una importante brecha por nivel socioeconómico en la esperanza de vida al nacimiento, con los hombres y mujeres de áreas de nivel socioeconómico más alto viviendo 3,8 y 3,2 años más, respectivamente, que en las áreas de nivel socioeconómico más bajo (Figura 13).

Figura 13. Esperanza de vida (en años) al nacimiento por sexo (A: hombres, B: mujeres) y quintil de privación en España, 2011-2013.



Además, la esperanza de vida es mayor en Madrid y en el norte de la España peninsular (Figura 14), zonas que en general tiene un alto nivel socioeconómico.

Figura 14. Quintiles de esperanza de vida (en años) al nacimiento por provincia y sexo (A: hombres, B: mujeres). España, 2011-2013.

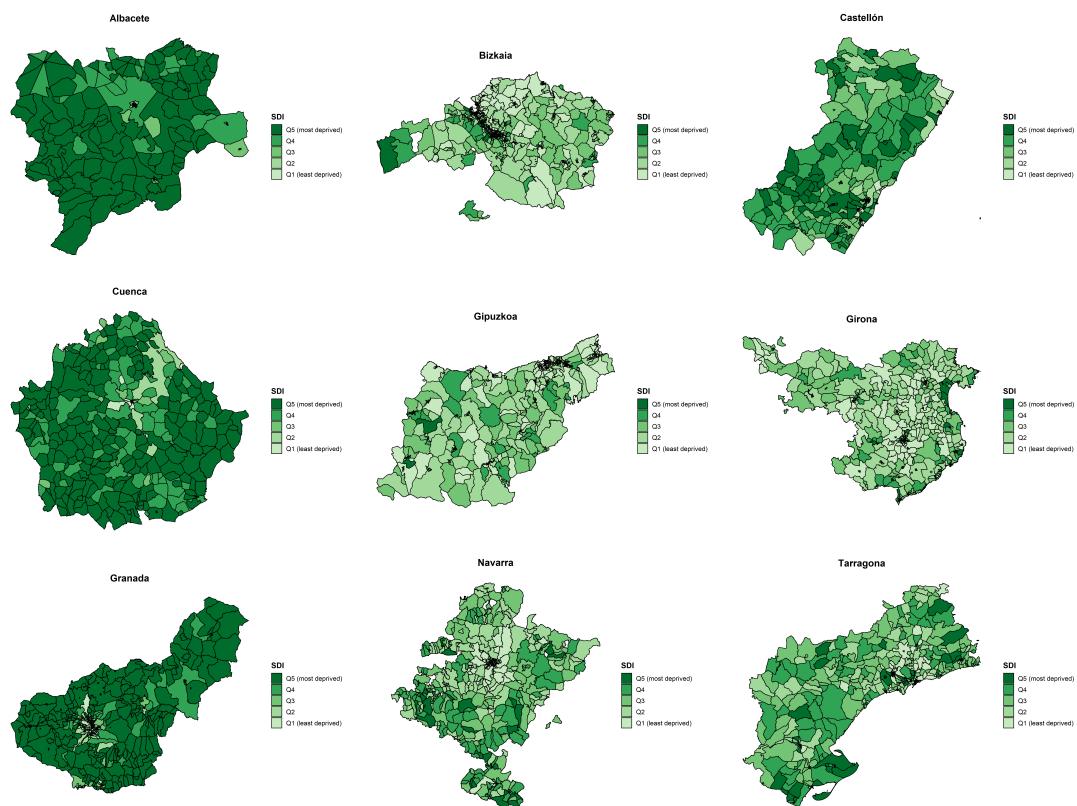


Finalmente, las tablas de vida para España por nivel socioeconómico, provincia, sexo y grupo de edad generadas están disponibles de forma abierta en GitHub [77] para facilitar su uso a personal investigador interesado. Un análisis preliminar sobre la supervivencia de cáncer de mama por nivel socioeconómico, empleando estas tablas de vida, está disponible en el Anexo 1.

4.3. Resultados del objetivo específico 3

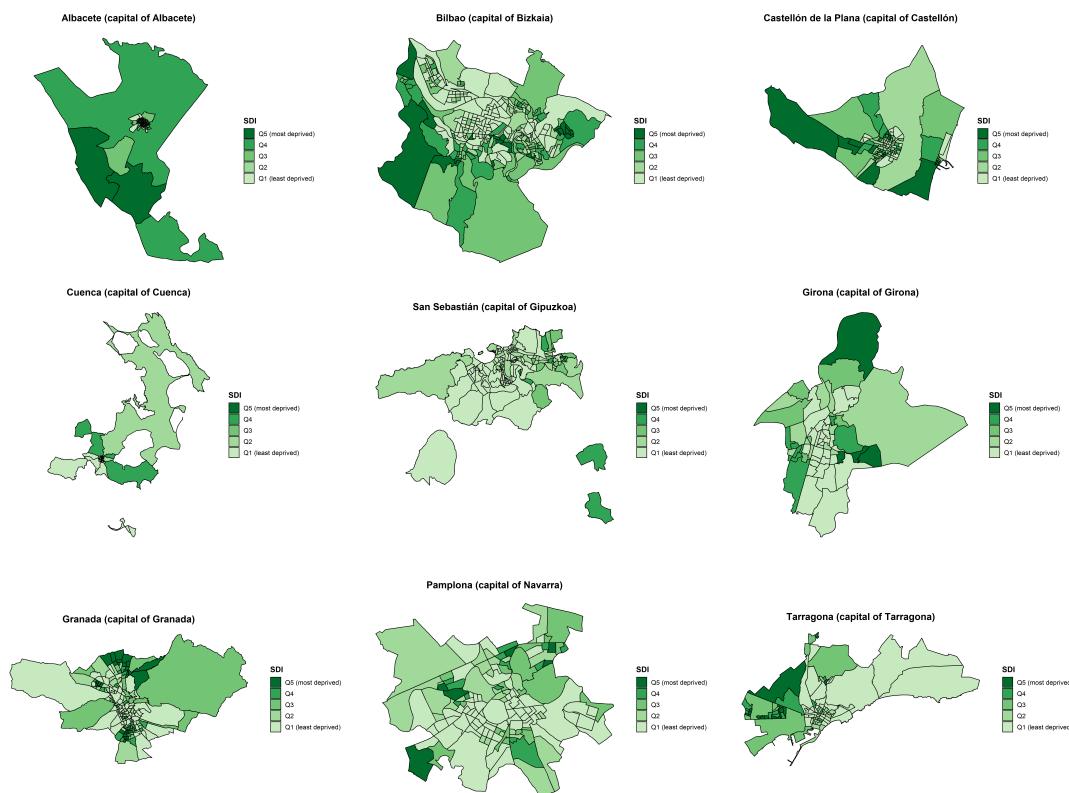
Entre las 9 provincias que participan en el estudio, el nivel socioeconómico fue más bajo en las provincias del sur de España (Albacete, Cuenca y Granada) comparadas con las del norte (Bizkaia, Gipuzkoa, Girona, Navarra y Tarragona), con Castellón mostrando un patrón intermedio (Figura 15).

Figura 15. Quintiles del índice de privación por sección censal en las 9 provincias del estudio, 2011.



En las capitales de provincia de las 9 provincias, formadas por zonas generalmente urbanas, el nivel socioeconómico fue alto, existiendo algunos barrios de la periferia con nivel socioeconómico bajo (Figura 16).

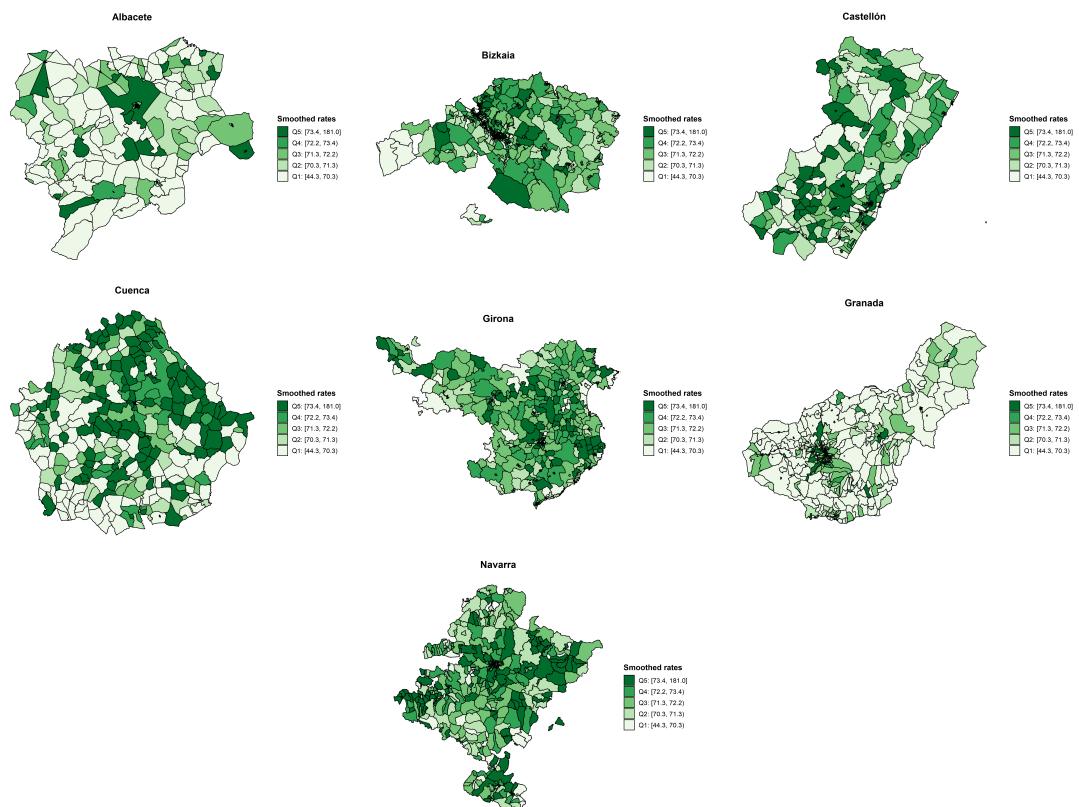
Figura 16. Quintiles del índice de privación por sección censal en las 9 capitales de provincia del estudio, 2011.



Para el cáncer de colon-recto, se analizaron 3.823 casos en 7 provincias, encontrando una mayor incidencia entre hombres de nivel socioeconómico más alto tras ajustar por edad y año de diagnóstico. Para mujeres no se encontró ninguna asociación entre nivel socioeconómico e incidencia de cáncer de colon-recto.

En las tasas suavizadas de incidencia de cáncer de colon-recto para ambos sexos (Figura 17) se encuentra un patrón norte-sur, con mayor incidencia en las provincias del norte de España (Bizkaia, Girona y Navarra).

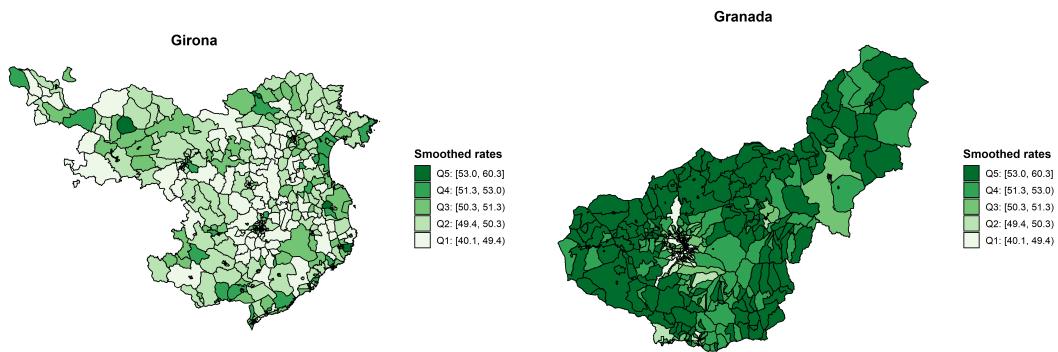
Figura 17. Tasas suavizadas de incidencia de cáncer de colon-recto ajustadas por nivel socioeconómico y edad. Ambos sexos.



De los 1.067 casos de cáncer de pulmón en Granada y Girona, el patrón de desigualdades socioeconómicas depende del sexo. Aunque había pocos casos y los intervalos de confianza fueron amplios, existe una incidencia mayor en hombres de bajo nivel socioeconómico y mujeres de alto nivel socioeconómico.

La incidencia de cáncer de pulmón en ambos sexos fue mayor en las zonas rurales de Granada (Figura 18).

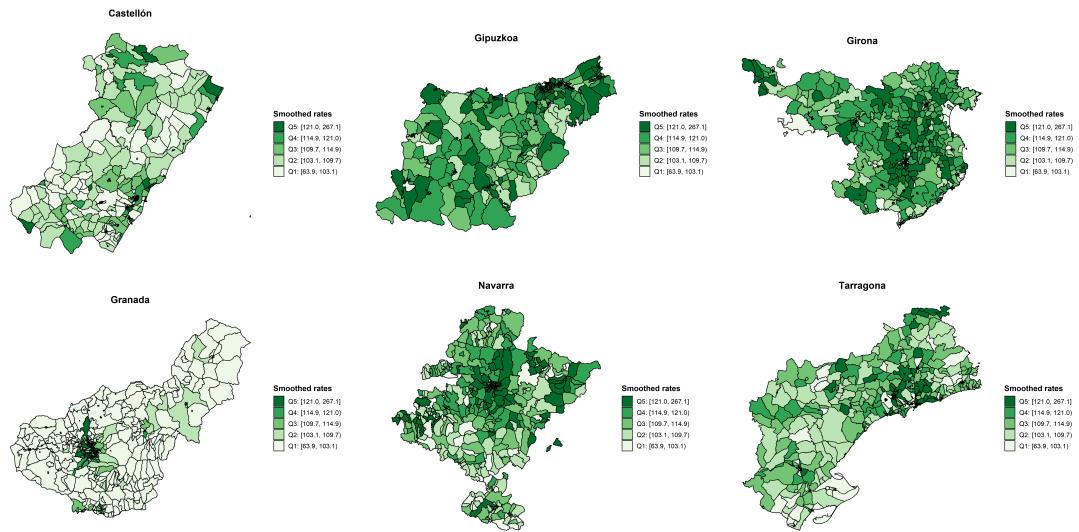
Figura 18. Tasas suavizadas de incidencia de cáncer de pulmón ajustadas por nivel socioeconómico y edad. Ambos sexos.



Para cáncer de mama en mujeres se analizaron 3.157 casos, hallando una mayor incidencia entre mujeres de alto nivel socioeconómico. Además, existía un claro gradiente de incidencia entre quintiles de privación.

Este resultado se hace visible al observar los mapas de incidencia suavizada, donde las provincias del norte y capitales de provincia tienen una mayor incidencia de cáncer de mama (Figura 19).

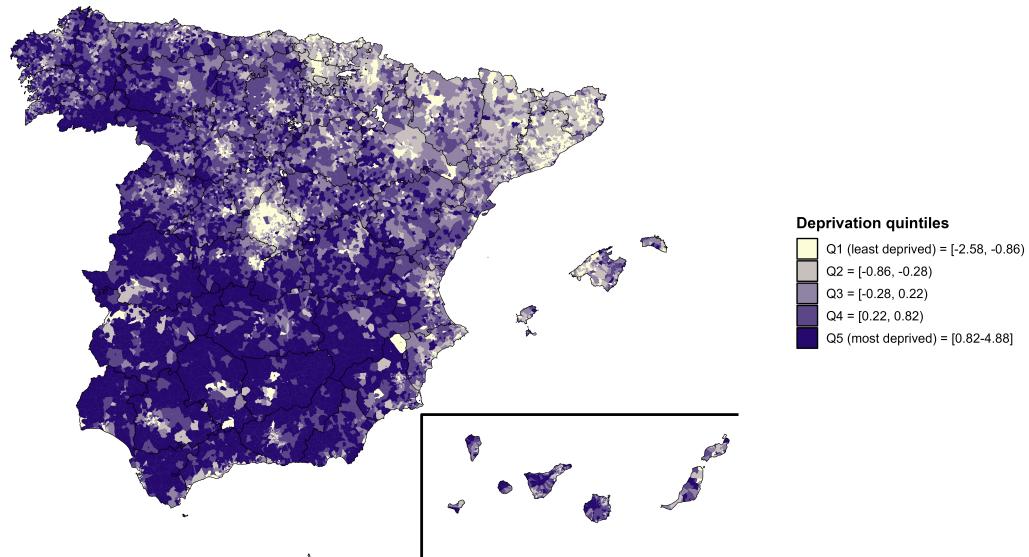
Figura 19. Tasas suavizadas de incidencia de cáncer de mama en mujeres ajustadas por nivel socioeconómico y edad.



4.4. Resultados del objetivo específico 4

La distribución geográfica del índice de privación por sección censal se muestra en la Figura 20. Existe un patrón norte-sur, con una privación menor (mayor nivel socioeconómico) en el noreste de España, la ciudad de Madrid y su área metropolitana.

Figura 20. Quintiles del índice de privación por sección censal.



Durante el periodo 2011-2017, se registraron en España 151.182 defunciones por cáncer de pulmón. La mortalidad por cáncer de pulmón fue mayor en hombres que en mujeres, con una razón de ASR-E de 5,3. El patrón espacial de la mortalidad fue muy diferente según el sexo (Figura 21).

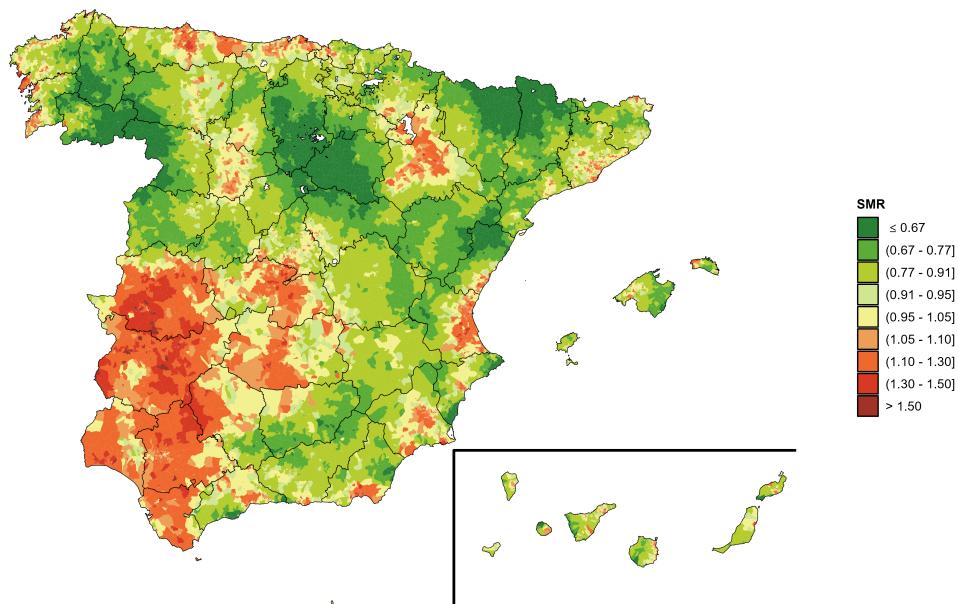
En hombres (Figura 21A), la mortalidad por cáncer de pulmón fue más alta en el suroeste, Zaragoza y Valencia. Las áreas con menor mortalidad estaban en el norte de España (Huesca, Lleida, Soria, Burgos, Zamora y Ourense).

La mortalidad por cáncer de pulmón en mujeres (Figura 21B) fue más alta principalmente en 3 zonas, una en Madrid y dos en el norte de la península (Asturias, Vizcaya, Álava, Gipuzkoa y Navarra). La mitad inferior de la península y el noroeste tuvieron una menor mortalidad por cáncer de pulmón en mujeres.

Figura 21. Razón suavizada estandarizada de mortalidad por cáncer de pulmón por sexo (A: hombres, B: mujeres). España, 2011-2017.

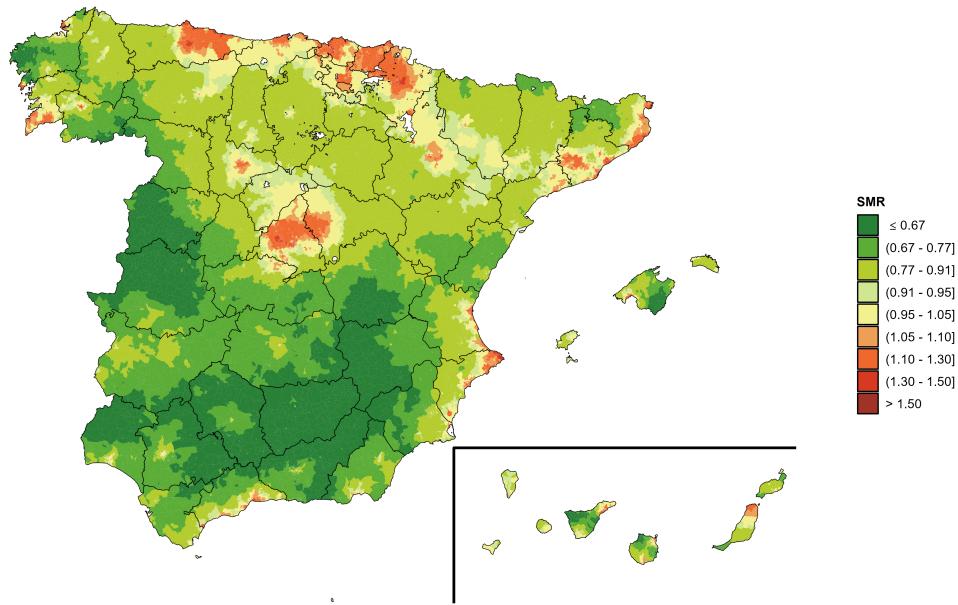
A

Lung cancer mortality.
Men, Spain, 2011-2017.



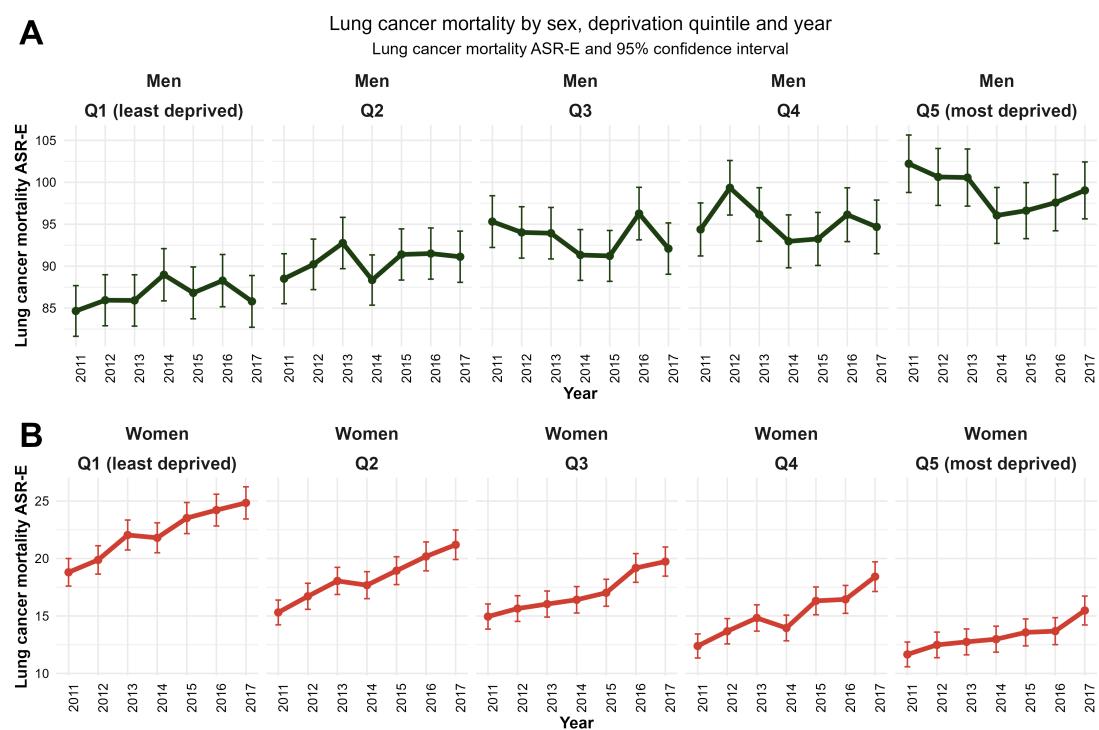
B

Lung cancer mortality.
Women, Spain, 2011-2017.



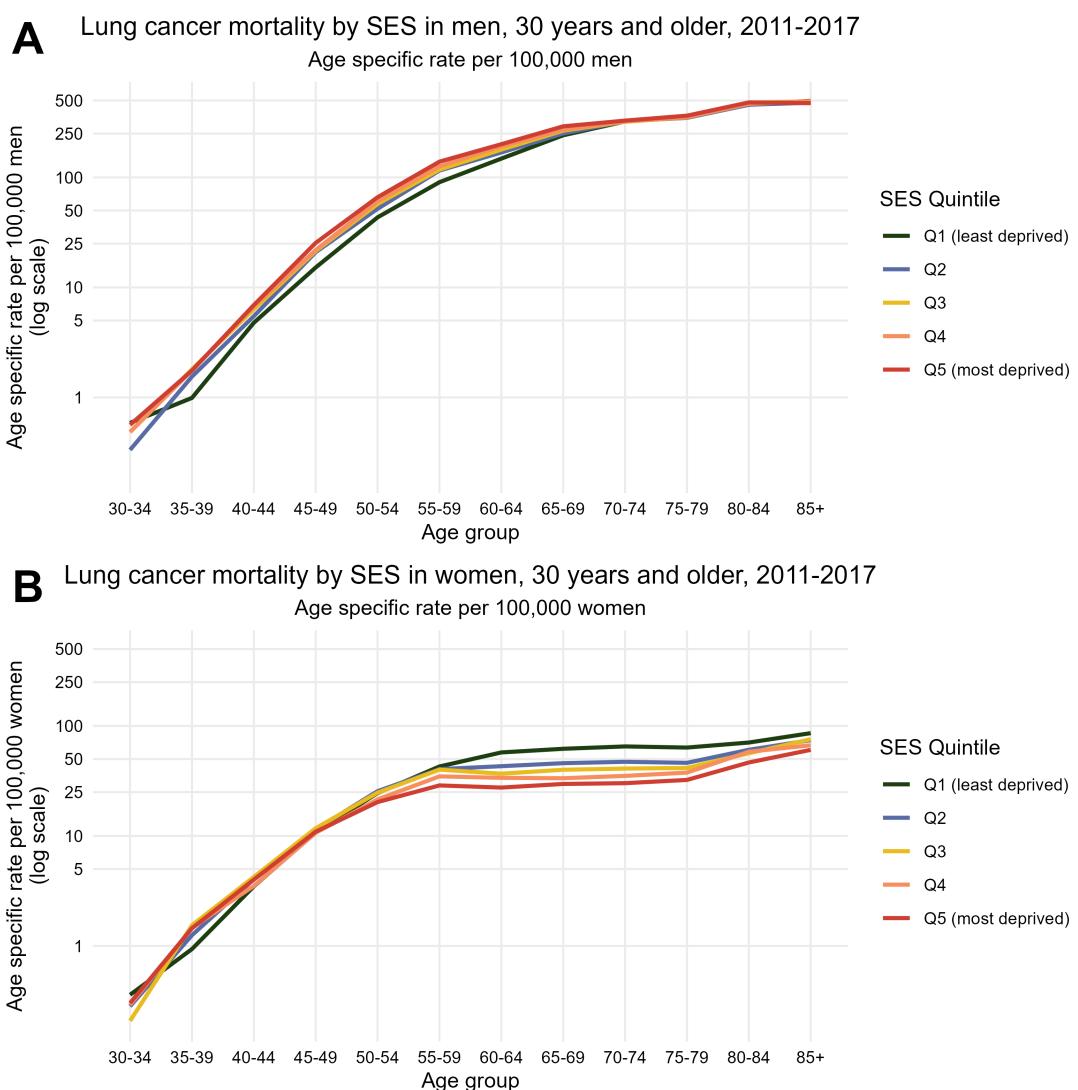
El impacto del nivel socioeconómico en la mortalidad por cáncer de pulmón fue claro aunque diferente para hombres y mujeres. Tuvieron mayor mortalidad por cáncer de pulmón las mujeres residentes en áreas de alto nivel socioeconómico y los hombres de áreas de bajo nivel socioeconómico. Este efecto fue consistente a lo largo del periodo de estudio (Figura 22).

Figura 22. Mortalidad por cáncer de pulmón por sexo, quintil de privación y año. ASR-E por 100.000 habitantes e intervalo de confianza al 95 %. España, 2011-2017.



Las desigualdades socioeconómicas encontradas en la mortalidad por cáncer de pulmón no afectaron por igual a todos los grupos de edad (Figura 23), siendo más claras entre los 35 y 69 años en hombres y a partir de los 50 años en mujeres.

Figura 23. Mortalidad por cáncer de pulmón por sexo (A: hombres, B: mujeres), grupo de edad y quintil de privación para adultos ≥ 30 años. Tasa específica por edad por 100.000 habitantes, escala logarítmica. España, 2011-2017.



En el Anexo 2 se ha realizado un análisis del impacto del nivel socioeconómico en la mortalidad por cáncer de colon-recto y mama.

Discusión

En este apartado se discute la metodología empleada y los resultados obtenidos en cada una de las publicaciones científicas asociadas a esta tesis doctoral. Una discusión más profunda se puede encontrar en el apartado de las publicaciones asociadas a la tesis doctoral (página [123](#)).

5.1. Artículo 1

En el primer artículo científico asociado a esta tesis doctoral (“*Socio-Economic Inequalities in Lung Cancer Outcomes: An Overview of Systematic Reviews*”) se encuentran importantes desigualdades socioeconómicas en relación con múltiples aspectos del cáncer de pulmón.

Pese a que no se ha podido incluir ninguna revisión sistemática que relacione el nivel socioeconómico con la incidencia de cáncer de pulmón, existen dos revisiones relevantes sobre este tema que no cumplieron los criterios de selección [\[98, 99\]](#) al no incluir una evaluación del riesgo de sesgo. En ambas revisiones se encontró una mayor incidencia de cáncer de pulmón entre las personas de nivel socioeconómico más bajo, incluso tras ajustar por hábito tabáquico.

En relación con la mortalidad, el trabajo de Wang et al. [\[91\]](#), que encontraba una mayor mortalidad en personas que tuvieron un nivel socioeconómico más bajo durante su infancia, se trataba de un pre-print que no había sido revisado externamente, aunque sus resultados estaban respaldados por una

revisión rápida [100]. Tras la publicación de nuestro estudio, el trabajo de Wang et al. ha sido publicado en la revista *Frontiers in Public Health* [101], no existiendo diferencias importantes entre los resultados de la versión pre-print y la versión definitiva.

Si bien no se encontraron diferencias en la duración de diferentes intervalos de cuidados por nivel socioeconómico, la duración de los intervalos temporales se reporta y analiza de formas muy diversas, lo que dificulta un resumen adecuado de los resultados en una revisión sistemática [102]. Además, los resultados pueden estar sesgados si el estado de salud de los pacientes no se tiene en cuenta, ya que puede influir en la definición estos intervalos [93]. Por tanto, el impacto del nivel socioeconómico en este tipo de indicador debería volver a analizarse cuando exista evidencia científica disponible de mayor calidad.

Tampoco se encontraron diferencias entre el nivel socioeconómico y el estadio al diagnóstico [93], algo que subraya la influencia limitada del nivel socioeconómico en el estadio, en consonancia con otros estudios [63, 95].

Con una mayoría de estudios originales de Estados Unidos, se encontraron evidencias de que las personas de nivel socioeconómico más bajo participaban menos en el cribado del cáncer de pulmón [92] y tenían más probabilidad de ser diagnosticados en situación de emergencia [93, 94]. El cribado de cáncer de pulmón mediante el uso de tomografía computarizada de baja dosis está implementado en algunos países (como Estados Unidos, Corea del Sur o Polonia) y está poniéndose en marcha en muchos otros (Canadá, Reino Unido, Alemania, Italia, España...) [103, 104]. Según algunos de los estudios realizados, este tipo de cribado reduce la mortalidad por cáncer de pulmón un 20-24 % [105, 106], aunque las personas de nivel socioeconómico más bajo parecen estar infrarrepresentadas en el cribado [107].

Los pacientes de cáncer de pulmón de nivel socioeconómico más bajo recibieron menos tratamientos, tanto tradicionales [95] como de nueva generación [96]. Aunque para estos últimos se necesita más investigación, una

revisión reciente sugiere que los tratamientos más novedosos tardan más en llegar a los pacientes de nivel socioeconómico más bajo [108].

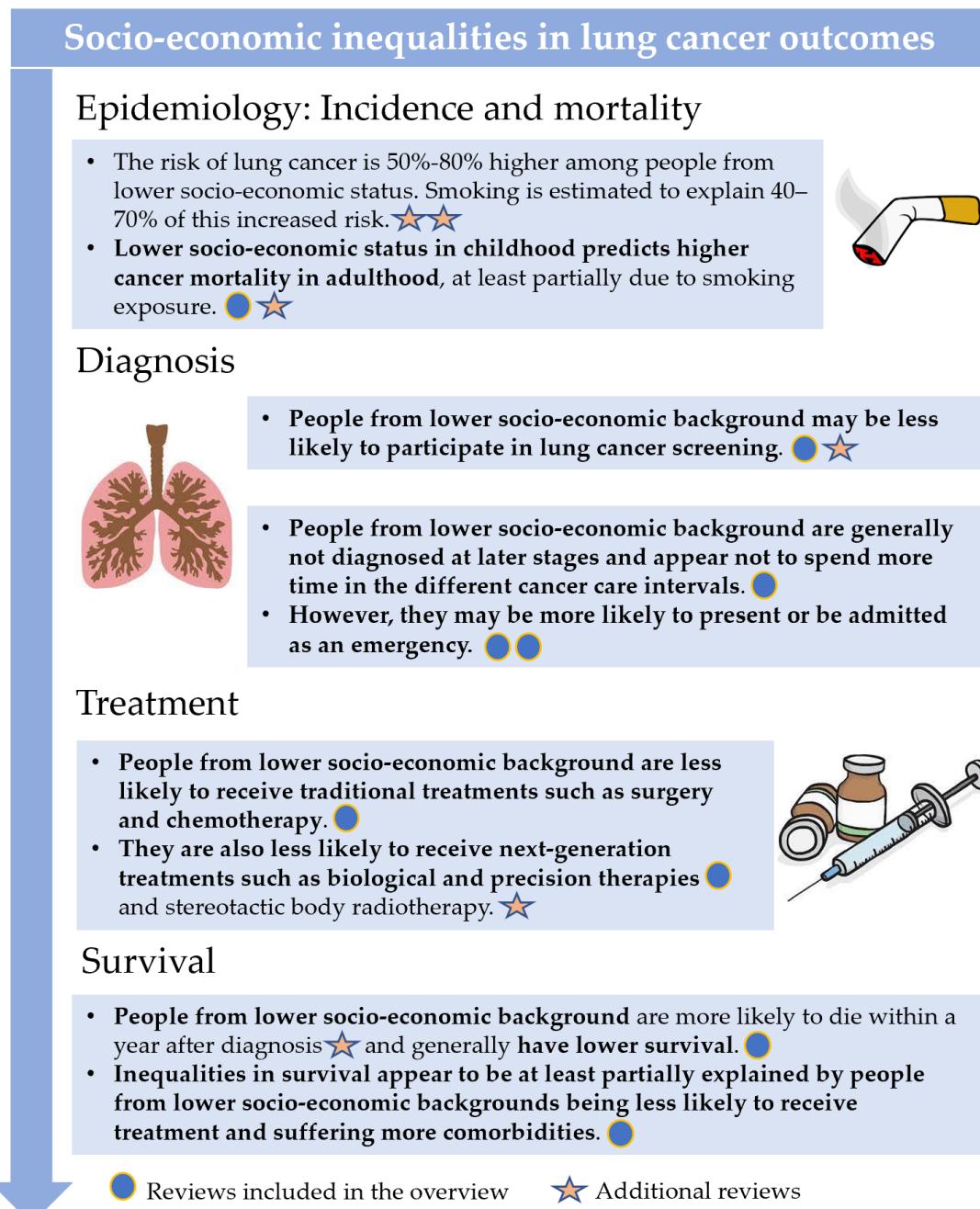
La mayor evidencia del estudio se encontró para la menor supervivencia en pacientes de cáncer de pulmón de bajo nivel socioeconómico, con 94 estudios en todo el mundo [97]. La mortalidad a corto plazo también se ve afectada por el nivel socioeconómico [109], siendo la diferencia en tratamientos y las comorbilidades las principales causas [50].

La principal limitación del estudio es que se usó una definición de “revisión sistemática” (la de Martinic et al. [74]) algo restrictiva, que dejaba fuera algunas revisiones sistemáticas relevantes. Según esta definición, las revisiones debían explicitar las siguientes características para ser calificadas como sistemáticas:

1. Pregunta de investigación.
2. Fuentes de información en las que se buscó, con una estrategia de búsqueda reproducible.
3. Criterios de inclusión y exclusión.
4. Métodos de selección.
5. Evaluación crítica de la calidad de los estudios originales incluidos.
6. Información sobre el análisis de datos y la síntesis que permita la reproducibilidad de los resultados.

Si bien algunas características se encontraban en casi todas las revisiones (pregunta de investigación, o criterios de inclusión/exclusión), otros aspectos (como la evaluación de la calidad de los estudios, o la estrategia de búsqueda totalmente reproducible) estuvieron menos presentes. Para tener en cuenta los resultados de los estudios excluidos relevantes se han incluido en la Figura 24, donde se resumen los principales resultados con respecto a desigualdades socioeconómicas en cáncer de pulmón.

Figura 24. Resumen de la evidencia disponible sobre desigualdades socioeconómicas en resultados de cáncer de pulmón.



Las desigualdades socioeconómicas encontradas hacen necesaria la aplicación de políticas a varios niveles, desde la prevención del cáncer de pulmón hasta la mejora de la supervivencia.

5.2. Artículo 2

En el artículo 2 (“*Association of socioeconomic deprivation with life expectancy and all-cause mortality in Spain, 2011–2013*”) se encontraron importantes desigualdades socioeconómicas en la esperanza de vida en España.

Los resultados del artículo son consistentes con un estudio previo que analizó la mortalidad general en 33 ciudades españolas usando áreas pequeñas [110] y también con las estadísticas oficiales a nivel nacional y europeo [111]. El patrón geográfico norte-sur encontrado, con mayor esperanza de vida en el norte, está bien documentado en otro estudio que concluye que la latitud geográfica guarda una relación directa con la mortalidad general en España [112]. También en Reino Unido se ha encontrado este patrón geográfico norte-sur, explicado principalmente por la privación socioeconómica [113].

Con respecto a la esperanza de vida por nivel socioeconómico, los resultados obtenidos están en línea con lo conocido en otros países europeos [113–115]. En Portugal, los resultados fueron muy similares, con los hombres y mujeres de niveles socioeconómicos más bajos viviendo 2,1 y 0,9 años menos, respectivamente [114]. En Reino Unido, la diferencia en esperanza de vida entre el nivel socioeconómico más alto y el más bajo se situaba entre 2,7 y 5 años en hombres y entre 2,5 y 3,6 años en mujeres [113]. Otros estudios en Noruega [116], Dinamarca [117], Bélgica [118], Estados Unidos [119] y Canadá [120] han encontrado una menor esperanza de vida en personas con menor nivel educativo o de ingresos.

Las principales limitaciones del estudio son tres:

1. El índice de privación utilizado [60] estaba referido al año 2011, mientras que la mortalidad analizada fue del periodo 2011-2013. La falta de

disponibilidad del índice de privación para años más recientes se debe a que está basado en el Censo de Población y Viviendas, que se realiza cada 10 años. Otro tipo de medida más actualizada adecuada al contexto español sería de gran utilidad para evaluar tendencias y cambios temporales del impacto del nivel socioeconómico en la mortalidad.

2. Por otro lado, el continuo cambio a lo largo del tiempo del seccionando censal representa una limitación. Por este motivo, en el cruce entre datos (privación/nivel socioeconómico - población - mortalidad) se perdieron el 1,7 % de las defunciones, una media de 6.567 muertes al año.
3. Para medir el nivel socioeconómico de las personas solo se ha podido considerar la sección censal de residencia en el momento de su muerte, lo que puede tener limitaciones especialmente en población anciana que haya cambiado de residencia en sus últimos años de vida.

Entre las fortalezas del estudio destaca el análisis exhaustivo de la mortalidad de España al completo durante 3 años. Otra fortaleza reside en la consistencia de los resultados obtenidos con los disponibles en otras regiones. Este es el primer estudio que evalúa la esperanza de vida al nacimiento por sexo y nivel socioeconómico en España, por lo que es un estudio relevante para el desarrollo de políticas de salud pública que busquen reducir las desigualdades encontradas. Por otro lado, las tablas de vida generadas durante el análisis están disponibles públicamente en GitHub [77], facilitando su uso para futuras investigaciones.

5.3. Artículo 3

En el tercer artículo (“*Lung, Breast and Colorectal Cancer Incidence by Socioeconomic Status in Spain: A Population-Based Multilevel Study*”) se encontraron importantes desigualdades socioeconómicas en la incidencia de cáncer de pulmón, mama y colon-recto en España.

Los resultados hallados en este trabajo son consistentes con la evidencia disponible de otros estudios de base poblacional en Europa [99].

Un bajo nivel socioeconómico estuvo asociado a una mayor incidencia de cáncer de pulmón en Dinamarca [121], Inglaterra [122, 123], Francia [124, 125], Alemania [126–128], Irlanda [129], Italia [130], Eslovenia [131], Suecia [132] y Escocia [133]. En el artículo 3 se encontró esa relación en hombres, aunque en mujeres no se observó ningún efecto del nivel socioeconómico, quizás debido al reducido número de casos y/o a la modificación del hábito tabáquico entre clases sociales a lo largo de las últimas décadas en la mujer (de clases altas en los años 70-80 a clases bajas actualmente).

Las mujeres de nivel socioeconómico más alto tuvieron más riesgo de cáncer de mama, en consonancia con otros estudios de Inglaterra [123], Francia [125], Alemania [126, 127], Irlanda [129], Italia [130], Escocia [134] y Eslovenia [131].

Los hombres de menor nivel socioeconómico tuvieron un mayor riesgo de cáncer de colon-recto. En Europa, la evidencia sobre este efecto es variable: algunos estudios encuentran una mayor incidencia de cáncer de colon-recto en niveles socioeconómicos más bajos [123, 127, 128, 133], mientras que otros estudios no observan asociación o incluso encuentran el efecto contrario [99, 124, 126, 129, 131, 135]. Esto puede deberse a la existencia de distintos patrones por nivel socioeconómico de estilos de vida en Europa [136] y al diferente impacto que han tenido los programas de cribado del cáncer de colon-recto [137].

Estudiar las causas de estas asociaciones podría ayudar a desarrollar medidas de salud pública adecuadas para la prevención del cáncer y la reducción de las desigualdades socioeconómicas en la incidencia del cáncer en España. Son necesarios más estudios colaborativos para actualizar la evaluación de las desigualdades socioeconómicas en el cáncer colorrectal, de pulmón y de mama a lo largo del tiempo en España y evaluar la efectividad de las medidas implantadas.

El estudio que se presenta en esta tesis ha sido el primer estudio que ana-

liza la asociación entre nivel socioeconómico e incidencia de cáncer usando datos poblacionales de cáncer de varias provincias españolas. Si bien estas provincias no cubrieron la totalidad del territorio español, la mayoría de los registros de cáncer españoles participaron en el estudio y el gradiente socioeconómico norte-sur estuvo bien representado.

Para no caer en la falacia ecológica, es importante notar que el índice de privación por sección censal no se utiliza como un proxy de nivel socioeconómico individual, sino como medida del efecto contextual de residir en una sección censal que tiene un determinado nivel socioeconómico. El índice de privación está referido al año 2011, mientras que los datos de incidencia son del periodo 2010-2013. Sin embargo, se puede argumentar que el nivel socioeconómico de un área es relativamente consistente a lo largo del tiempo [138].

5.4. Artículo 4

En el cuarto artículo asociado a la tesis doctoral (“*Socio-economic inequalities in lung cancer mortality in Spain: a nation-wide study using area-based deprivation*”) se encuentra una mayor mortalidad por cáncer de pulmón en hombres de nivel socioeconómico más bajo y en mujeres de nivel socioeconómico más alto.

La evidencia científica encontrada en hombres está bien documentada en múltiples estudios europeos que midieron el nivel socioeconómico tanto de forma individual como a nivel de área [59, 132, 139–156]. Para las mujeres, la asociación que se encontró es menos consistente en otros estudios y parece depender de la región analizada y, por tanto, del hábito tabáquico en mujeres. En países del oeste y norte de Europa, son las mujeres de niveles socioeconómicos más bajos quienes sufren una mayor mortalidad por cáncer de pulmón [132, 141, 144, 145]. El efecto contrario se ha encontrado en Italia [139] y en otros estudios de España [59, 149, 156]. De hecho, este patrón divergente en las regiones mediterráneas está documentado en estudios previos que consideraron distintas regiones europeas [143, 157, 158].

Dado el mal pronóstico del cáncer de pulmón (con una supervivencia neta a los 5 años de 13,2 % en España [46]) y el hecho de que el consumo de tabaco sea el principal factor de riesgo del cáncer de pulmón, se puede concluir que diferentes patrones de tabaquismo por nivel socioeconómico podrían ser la causa de las desigualdades encontradas en la mortalidad por cáncer de pulmón. Además, otros factores como problemas económicos, acceso a servicios de salud o marginación pueden afectar también a la mortalidad [65].

Los mapas de mortalidad por cáncer de pulmón muestran un patrón muy similar al encontrado en el Atlas de Mortalidad por Cáncer en España y Portugal [159], que analiza un periodo algo anterior (2003-2012) a nivel municipal, con una unidad de análisis más amplia.

Las desigualdades socioeconómicas encontradas en la mortalidad por cáncer de pulmón hacen necesario el desarrollo de intervenciones para reducirlas. Un seguimiento periódico de los indicadores de mortalidad por nivel socioeconómico permitiría una evaluación de la efectividad de las intervenciones realizadas. El Plan Europeo de Lucha contra el Cáncer promueve la implantación de un programa de cribado para el cáncer de pulmón mediante tomografía computarizada de baja dosis [160]. En España, varias sociedades científicas están pilotando el proyecto CASSANDRA (*Cancer Screening, Smoking Cessation and Respiratory Assessment*), cuyo objetivo es evaluar la viabilidad del cribado poblacional mediante el reclutamiento de pacientes en más de 20 centros públicos, privados y de atención primaria. La evaluación del programa de cribado del cáncer de pulmón por parte del Ministerio de Sanidad concluye que el cribado reduce ligeramente el riesgo de muerte en personas fumadoras y exfumadoras, pero no parece afectar a la mortalidad global [104]. Además, se detectan desigualdades en el acceso y la elegibilidad en ciertos grupos vulnerables como personas de bajo nivel socioeconómico y educativo [104]. Estudios previos sugieren que implementar nuevas intervenciones como el cribado del cáncer de pulmón pueden ampliar las desigualdades de mortalidad existentes [92, 161–163]. Una premisa clave del éxito del cribado del cáncer de pulmón es la identificación de perfiles de alto riesgo, que suele depender únicamente de datos sobre hábito tabáquico,

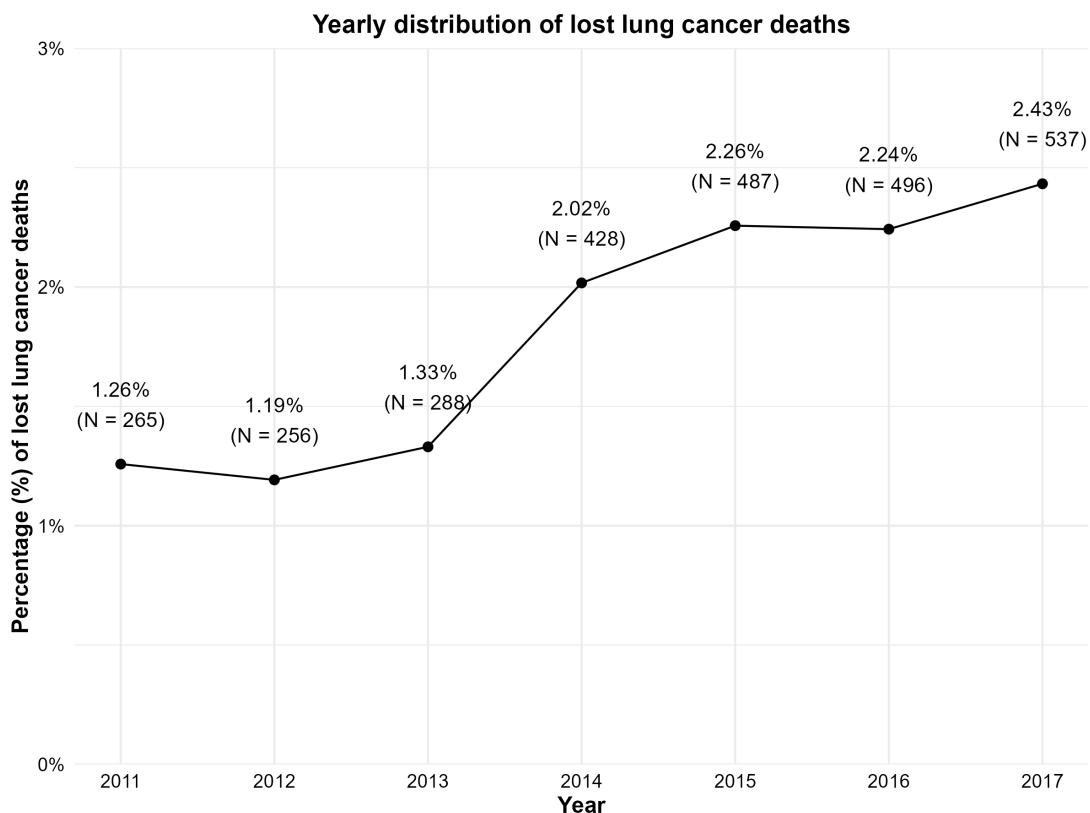
mientras que los resultados encontrados en este artículo sugieren que el nivel socioeconómico debe ser otro factor relevante a considerar.

Para reducir el alcance de las desigualdades socioeconómicas detectadas en nuestro estudio es necesario un enfoque complejo que incluya intervenciones, tanto a nivel individual como poblacional. La mejora del acceso a la asistencia sanitaria en los grupos socioeconómicos más bajos (especialmente en los hombres) y la reducción de la exposición a factores de riesgo como el tabaquismo o los contaminantes ambientales podrían reducir las desigualdades en la mortalidad por cáncer de pulmón, si bien se requiere un mayor conocimiento de las causas subyacentes para que las intervenciones sean más eficaces.

Una de las limitaciones reside en que el índice de privación está referido al año 2011 mientras que la mortalidad considerada cubre el periodo 2011-2017. El uso del Índice Europeo de Privación [57] habría facilitado la comparación con otros estudios europeos, pero desafortunadamente la última actualización de este índice para España corresponde al año 2001.

Por otra parte, al cruzar datos de distintas fuentes de información y años de referencia, un pequeño porcentaje de defunciones (menos del 2% global) se perdió debido a los cambios en el seccionado censal a lo largo del tiempo. En la Figura 25 se muestra la distribución de defunciones perdidas por año, que es más alta en los últimos años del periodo.

Figura 25. Porcentaje y número de defunciones perdidas por año tras el cruce de mortalidad por cáncer de pulmón con población y cartografía. España, 2011-2017.



La principal fortaleza del estudio es el uso de datos de mortalidad exhaustivos a nivel nacional, recogidos por una institución oficial. Aunque es posible que existan problemas con la codificación de la causa de muerte [164, 165], en el caso del cáncer de pulmón no es tan probable como en otras localizaciones anatómicas como el caso del cáncer de útero [43, 166].

Conclusiones

1. La evidencia científica disponible a nivel mundial muestra que el nivel socioeconómico influye en el cáncer de pulmón. Las personas de un nivel socioeconómico más bajo tienen mayor riesgo de desarrollar un cáncer de pulmón y de morir debido al tumor. Además, tienen una supervivencia más baja ya que reciben menos tratamientos que los pacientes de niveles socioeconómicos más altos, tienen más comorbilidades y mayor probabilidad de acudir a urgencias. Las desigualdades están presentes tanto midiendo el nivel socioeconómico de forma individual como usando medidas de área.
2. El nivel socioeconómico tiene un importante efecto en la esperanza de vida en España. Las personas del nivel socioeconómico más bajo tienen una esperanza de vida al nacimiento 3,2 años menor en mujeres y 3,8 años menor en hombres, comparados con el nivel socioeconómico más alto.
3. En España, el nivel socioeconómico influye en la incidencia de los cánceres de pulmón, colon-recto y mama, con el sentido y la magnitud del efecto dependiendo de la localización anatómica. Un nivel socioeconómico más bajo estuvo asociado con una mayor incidencia de cáncer de pulmón en hombres. En mujeres, un nivel socioeconómico más alto estuvo asociado con una mayor incidencia de cáncer de mama y una mayor incidencia de cáncer de pulmón. Para el cáncer de colon-recto, se encontró una mayor incidencia entre hombres de nivel socioeconómico más alto. Las desigualdades socioeconómicas encontradas son consis-

tentes con las de otros países europeos.

4. La mortalidad por cáncer de pulmón en España estuvo influenciada por el nivel socioeconómico. En hombres, un nivel socioeconómico más bajo estuvo asociado con una mayor mortalidad por cáncer de pulmón. En mujeres el patrón se revirtió: un nivel socioeconómico más alto estuvo asociado con una mayor mortalidad por cáncer de pulmón.

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Publicaciones científicas asociadas a la tesis doctoral

Artículo 1 - Socio-Economic Inequalities in Lung Cancer Outcomes: An Overview of Systematic Reviews

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Systematic Review

Socio-Economic Inequalities in Lung Cancer Outcomes: An Overview of Systematic Reviews

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Simple Summary: Lung cancer is the leading cause of cancer mortality worldwide. Research has revealed significant socio-economic inequalities in lung cancer, such that people of lower socio-economic status (SES) generally have worse outcomes. In this article, using the umbrella review methodology, we review and organize the available evidence on socio-economic inequalities in diverse lung cancer outcomes. We find that people of a lower SES have a lower chance of cancer survival, most likely due to the lower likelihood of receiving both traditional and next-generation treatments, higher rates of comorbidities, and higher likelihood of being admitted as emergency. People of a lower SES are generally not diagnosed at later stages, but this may change after broader implementation of lung cancer screening, as early evidence suggests that there are socio-economic inequalities in its use.

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Abstract: In the past decade, evidence has accumulated about socio-economic inequalities in very diverse lung cancer outcomes. To better understand the global effects of socio-economic factors in lung cancer, we conducted an overview of systematic reviews. Four databases were searched for systematic reviews reporting on the relationship between measures of socio-economic status (SES) (individual or area-based) and diverse lung cancer outcomes, including epidemiological indicators and diagnosis- and treatment-related variables. AMSTAR-2 was used to assess the quality of the selected systematic reviews. Eight systematic reviews based on 220 original studies and 8 different indicators were identified. Compared to people with a high SES, people with a lower SES appear to be more likely to develop and die from lung cancer. People with lower SES also have lower cancer survival, most likely due to the lower likelihood of receiving both traditional and next-generation treatments, higher rates of comorbidities, and the higher likelihood of being admitted as emergency. People with a lower SES are generally not diagnosed at later stages, but this may change after broader implementation of lung cancer screening, as early evidence suggests that there may be socio-economic inequalities in its use.

Keywords: lung cancer; socio-economic; disparities; inequalities; income; education; survival; treatment; diagnosis

1. Introduction

In 2020, lung cancer was the leading cause of cancer death worldwide, responsible for 18.2 percent of all cancer deaths, and the second most commonly diagnosed cancer for both sexes combined [1]. In men, lung cancer was the most commonly diagnosed cancer and the leading cause of cancer death [1]. In women, it was the third most commonly diagnosed malignancy and the second cause of cancer mortality [1].

Despite significant improvements in diagnosis and treatment in recent decades, lung cancer still has one of the lowest survival rates, with particularly low survival for individuals in advanced stages. Average five-year survival rates vary significantly between countries, with estimates ranging from 10% to 20% [2,3]. For instance, in Europe the average five-year age-standardized relative survival for lung cancer patients diagnosed between 2000 and 2007 was 13% according to EUROCARE-5 statistics [2,3].

Cancer outcomes are known to have an important social gradient and lung cancer is no exception. Factors such as socio-economic position, race, ethnicity, and place of residence have been found to produce social disparities in diverse cancer-related outcomes [4–8]. Among those, socio-economic status (SES) is a complex factor that can encompass several dimensions of the social and economic life circumstances of individuals and is often measured using information regarding education, income, and/or occupation [5].

Researchers have used diverse methodological approaches to the study of socio-economic disparities in cancer outcomes [5]. The individual approach uses information about each person's socio-economic position, whereas the ecological approach uses area-based aggregated information such as deprivation indices that consider demographic, social, and/or economic factors of the residence area [5]. The magnitude and type of disparities identified could vary strongly from one approach to the other. However, both approaches offer useful and complementary information, and most importantly, both approaches have identified striking disparities in lung cancer outcomes including incidence [9], treatment [10,11], early mortality [12], and survival [11,13]. For instance, lung cancer incidence is higher among people from lower socio-economic status, as indicated by education, income, or occupation [14], using both individual and area-based indicators [9], with relative risks generally in the range of 1.5 to 1.8.

The last two decades have brought about important improvements in lung cancer diagnosis and treatment [15]. However, recent evidence suggests that people with a lower SES could be less likely to benefit from such improvements. For instance, in the US, lower SES is associated with lower rates of lung cancer screening [16,17] and lower rates of utilization of last-generation therapies [18,19].

Given the increasing number of outcomes for which socio-economic disparities have been investigated, the goal of the current research was to conduct an umbrella review of systematic reviews and map the evidence available regarding the role of SES in lung cancer outcomes, considering the methodological quality of the systematic reviews available and the quantity of the evidence.

2. Materials and Methods

We conducted an umbrella review (i.e., overview of systematic reviews) following methodological recommendations by several authors [20–23]. The unit of analysis in umbrella reviews is the systematic review and a preferred reporting items checklist for umbrella reviews is still under development [24]. Hence, in reporting the review, we followed the PRIO-harms checklist [25], a checklist designed for overviews of systematic reviews, including harms, by ignoring the items not applicable to the topic of our review (e.g., pertaining superficially to harms). A protocol was pre-registered in PROSPERO (ID: CRD42021282194), specifying the following criteria:

Population: Adult patients (18 years old or older) diagnosed with lung cancer.

Exposure/comparator: Socioeconomic status, specifically reviews comparing outcomes between patients with relatively lower vs. higher socioeconomic status. Any measure of socioeconomic status was considered, including individual-level and area-based measures (e.g., based on income, education, occupation, or a mixture thereof, area deprivation indices, etc.).

Outcomes: Diverse lung cancer outcomes were considered: epidemiological indicators (e.g., incidence, mortality, survival) and outcomes related to the diagnosis and treatment of lung cancer (e.g., screening, utilization of tests and treatments).

Study design: Systematic reviews of observational studies reporting on the relationship between socioeconomic status and any of the lung cancer outcomes considered.

Exclusion criteria: Articles published in 2009 or earlier (this criterion was set to exclude reviews that do not include the latest evidence); reviews that focus on other types of disparities (e.g., based on gender, race, rural vs. urban residence, etc.); reviews that do not report results specific to lung cancer; reviews that report on the prevalence of smoking or other risk factors or other outcomes not directly related to the diagnosis or treatment of lung cancer; reviews that are in a language not spoken by the research team (i.e., not English, Spanish, German, Dutch, Portuguese, Russian, Bulgarian), or the full text of which cannot be obtained.

Finally, we excluded reviews that were not considered systematic as per the definition of Martinic et al. [26]. As per this definition, the reviews were required to have the following characteristics to qualify as systematic: (i) research question, (ii) sources that were searched, with a reproducible search strategy (naming of databases, naming of search platforms/engines, search date and complete search strategy), (iii) inclusion and exclusion criteria, (iv) selection (screening) methods, (v) critical appraisal and report of the quality/risk of bias of the included studies, (vi) information about data analysis and synthesis that allows the reproducibility of the results.

Search strategy: We searched Medline via PubMed, Scopus, and Web of Science from 2010 onwards until 26 October 2021. Google Scholar was also searched manually to locate dissertations, pre-prints, and other unpublished materials. There were no restrictions by language in the search. Additional studies were identified by reviewing the reference lists of relevant reviews identified from the search. The full search strategy is available as Supplementary Material on The Open Science Framework (OSF) (<http://doi.org/10.17605/OSF.IO/TS5G8> accessed on 13 January 2022).

Article selection and data extraction: The software Covidence (www.covidence.org, accessed on 13 January 2022) was used to manage all the stages of the review. Articles were screened based on title and abstract by two reviewers (D.P. and D.R.-S.). At this stage, articles receiving two “no” responses were excluded, whereas the rest (one or two “yes” responses) proceeded to full text review. Two reviewers (D.P. and D.R.-S.) read the full text of each article against the inclusion and exclusion criteria and disagreements were resolved through discussion. The reason for exclusion was recorded for each article.

Data was extracted from the articles selected for inclusion using a pre-defined form in Covidence by one reviewer (D.P.) and was then thoroughly checked by another reviewer (D.R.-S.). Per protocol, these data included: article title, first author, year of publication, type of measure of socioeconomic status used, lung cancer outcome studied, inclusion and exclusion criteria for original studies, dates covered by the literature search, number of original studies (k) and participants (n) included in the review, main results regarding the outcomes of interest (meta-analytic results with confidence interval estimates, *p*-values, and *I*² values were extracted whenever available), and main limitations of the review. In addition to the data items pre-specified in the protocol, we extracted information about the geographical representation of the included studies, the reported funding of each review, whether the authors declared potential conflicts of interest, what instruments were used to evaluate the methodological quality of the original studies included in each review, and whether the reported analysis and conclusions were based on adjusted or unadjusted models.

Risk of bias: The risk of bias of the included reviews was assessed independently by two authors using the AMSTAR-2 checklist [27]. Disagreements were resolved through discussion. The AMSTAR-2 consists of 16 items that assess the rigor of systematic reviews of non-randomized studies on several domains, from which we considered five as critical for the current context: (i) whether a protocol was registered before the start of the review, (ii) adequacy of the literature search, (iii) risk of bias from individual studies included in the review, (iv) appropriateness of the meta-analytical methods used, and (v) consideration of this risk of bias in the interpretation of the results [27]. The results of individual items are not meant to be combined in a total score, instead, overall confidence in each review can be judged (e.g., high, moderate, low) based on weaknesses detected in critical and non-critical items [27]. We rated the reviews as follows: “high confidence” reviews had no weaknesses on any of the five critical domains and had no or only one weakness in a non-critical domain; “moderate confidence” reviews had no weaknesses on any of the critical domains but could have more than one non-critical weakness; and “low confidence” reviews had more than one critical weakness regardless of the number of non-critical weaknesses.

Data synthesis: Meta-analysis was not planned (nor meaningful for such a diverse set of outcomes). Results were synthesized narratively, considering the amount of the available evidence and the risk of bias of each review. In case of substantial overlap in the included original studies between two reviews (e.g., an older and more recent review on a very similar topic), the more recent and complete review was to be given more weight in the results.

3. Results

The flowchart of article selection is displayed in Figure 1. From 267 initial records, eight systematic reviews were included. The main reasons for exclusion for each article at the full-text stage are available as supplementary material on OSF (<http://doi.org/10.17605/OSF.IO/TS5G8>, accessed on 13 January 2022) (some articles could be excluded for more than one reason, but the software only permitted recording one).

Table 1 reports the main characteristics and results of the included studies and Table 2 reports information about the covariate adjustment, risk of bias assessment, and methodological limitations of each review. Table S1 on OSF (<http://doi.org/10.17605/OSF.IO/TS5G8>, accessed on 13 January 2022) reports additional review information including detailed inclusion and exclusion criteria, review funding sources, and conflicts of interest.

Overall, the eight systematic reviews reported on 220 non-overlapping original studies examining eight types of outcomes, including mortality, survival, screening utilization, cancer care interval duration, emergency presentation, stage at diagnosis, test use, and treatment receipt. Almost all original studies included in the reviews stemmed from high income countries (e.g., US, UK, European Union, and Australia).

The risk of bias ratings for each item of the AMSTAR-2 is displayed in Figure 2. Overall, four reviews were classified as “moderate confidence” and four as “low confidence”.

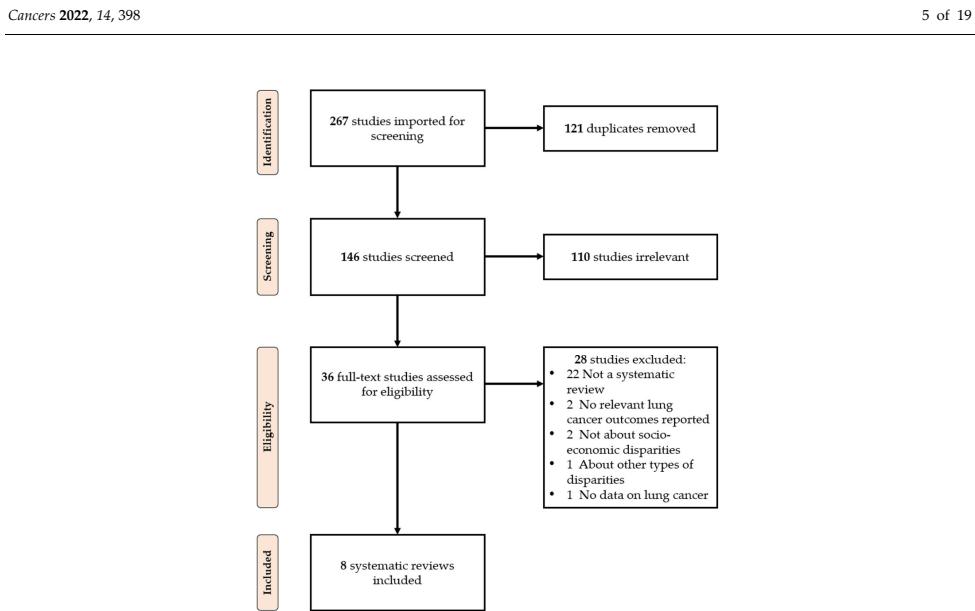


Figure 1. PRISMA flowchart of the review selection process.

N: No; NA: Not available because no meta-analysis was done; PY: Partial Yes; Y: Yes

* Critical item of AMSTAR-2

Figure 2. Risk of bias ratings for each item of the AMSTAR-2.

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Table 1. Main characteristics and results of the included reviews.

| First Author and Pub. Year | Measure(s) of SES | Lung Cancer Outcomes(s) | Search Period | Number of Original Studies Included (k) | Geographical Representation of the Included Studies | Total Number of Participants/Patients | Main Results Regarding the Outcomes of Interest |
|----------------------------|-----------------------------------|--|---------------|--|---|---|---|
| Afshar 2021 | Diverse individual and area-based | Survival (cancer-specific and overall) | 2005–2020 | 7 | UK (k = 3), Denmark (k = 1), Germany (k = 1), Sweden (k = 1), and US (k = 1) | 111,275 | Inequalities in survival appear to be partly explained by receipt of treatment and co-morbidities. Results regarding the mediating role of stage at diagnosis were mixed. No meta-analysis was performed. Individual measures: There was no effect of education (HR = 1.03 (0.96, 1.10, ref = high education), I ² = 55%, k = 13). Lower income was associated with lower survival (HR = 1.13 (1.08, 1.19), ref = high income), I ² = 0%, k = 7). Occupations associated with lower SES did not show lower survival (k = 3), no meta-analysis. Area-based measures: Education (k = 3), income (k = 19), SES-index (k = 22). No meta-analyses could be conducted overall but results were generally consistent with lower survival among patients residing in lower SES areas. |
| Finke 2018 | Diverse individual and area-based | Survival | Start–2017 | 94 (23 based on individual measures and 70 mostly from Scandinavia, on area-based measures, 1 on both levels), 17 mostly from US, UK, and included in Australia/New Zealand meta-analysis. | Individual measures: Individual measures; >187,000 in studies with individual measures; >4,250,000 in studies with area-based measures. | >187,000 in studies with individual measures; >4,250,000 in studies with area-based measures. | Comparison: The range of differences between survival rates for lowest and highest SES groups was larger in studies considering area-based SES than in studies assessing individual SES (Individual SES: range 1.0–12.8% units; area-based SES: range 0.9–22.9% units) but did not depend on the SES measure or the population size of the area. |
| Forrest 2013 | Diverse individual and area-based | Receipt of treatment (surgery, chemotherapy, radiotherapy, | start–2012 | 46 (1 based on an individual measure and 45 on area-based measures of SES) | US (k = 18), UK (k = 19), Canada (k = 2), Sweden (k = 1), Australia (k = 1), | Surgery: >656,000 Chemotherapy: >359,000 Radiotherapy: >235,000 | Overall: Lower SES was associated with lower likelihood of receiving treatment: OR = 0.79 [95% CI 0.73 to 0.86], p < 0.001, I ² = 77%, k = 26. Surgery: Patients of lower SES were less likely to undergo surgery: OR = 0.72 (95% CI 0.65 to 0.80), p < |

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|-----------------------|-----------------------------------|---|--|--|---|---|---|
| | | unspecified treatment) | Italy (k = 1), France (k = 1), and New Zealand (k = 3) | Unspecified treatment: >115,000 | 0.001, I ² = 80%, k = 16 (also when controlling for histology and stage at diagnosis). | Chemotherapy: Patients with lower SES were less likely to undergo chemotherapy, OR = 0.81 [95% CI 0.73 to 0.89], p < 0.001, I ² = 68%, k = 10. | Radiotherapy: There was no association of SES with the receipt of radiotherapy, OR = 0.99 [95% CI 0.86 to 1.14], p = 0.89, I ² = 54%, k = 7. |
| | | Stage (at diagnosis or start of treatment); duration of time intervals on the lung cancer pathway | 39 (23 for stage, 12 for intervals, and 8 for proxy measures of delay) | UK (k = 20), US (k = 10), Canada (k = 2), Denmark (k = 2), Sweden (k = 1), Australia (k = 1), Italy (k = 1), Korea (k = 1), and New Zealand (k = 1). | >267,500 for stage, >79,700 for intervals, >569,100 for proxy measures | Unspecified treatment type: Patients with lower SES were less likely to receive treatment, OR = 0.78 [95% CI 0.74 to 0.83], p < 0.001, I ² = 0, k = 5. | Stage: There was no evidence of socio-economic inequalities in late stage at diagnosis in the most, compared with the least, deprived groups (OR = 1.04, 95% CI = 0.92 to 1.19, I ² = 60%, k = 7). Studies that were not suitable for meta-analysis (k = 16) showed the same pattern of results. |
| Forrest 2017 | Diverse individual and area-based | Emergency presentation: a diagnosis of cancer that arose | start-2016 | UK (k = 3), US (k = 1) | 163,050 | Higher socio-economic deprivation (as measured by area-based indices) increased the likelihood of emergency presentation in all 3 studies identified. There | Intervals: 12 studies examined 8 intervals from the cancer care pathway (e.g., patient interval, GP referral interval, diagnostic interval, etc.). There was no evidence of socio-economic inequalities. No meta-analysis was performed. Proxy measures of delay: These included acute presentation, emergency admission, number of times to consult and diagnosis at death (k = 8). More deprived patients were more likely to present and to be admitted as an emergency, but socio-economic inequalities were not found in the number of times to consult or in diagnosis at death. |

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|-----------------------|--|---|------------|---|---|--|--|
| | | | | | | | was no association between annual household income and emergency presentation in the one study identified. No meta-analysis was conducted. |
| Norris 2020 | Diverse individual and area-based (the large majority area-based) | Utilization of predictive biomarker tests and biological and precision therapies | 1998–2019 | 11 (2 on predictive biomarkers and 9 on biological and precision therapies) | US (k = 11) | 505,105 (15,588 for biomarker tests and 534,517 for therapy) | Predictive biomarkers: There was no relationship between SES and utilization of predictive biomarker tests (epidermal growth factor receptor and/or anaesthetic lymphoma kinase): OR = 0.92 (95% CI 0.35, 2.40), $P = 97\%$, $k = 2$ (the two studies found relationships in the opposite direction). Biological and precision therapies: Lower SES was related to lower utilization of these therapies, OR = 0.71 (95% CI 0.51, 1.00), $I^2 = 95\%$, $k = 6$ (low compared to high SES). |
| Sosa 2021 | Individual income and education | Screening eligibility; screening completion/intention; late stage diagnosis; lung cancer-specific mortality | 2010–2020 | 6 | US (k = 6) | 163,418 | Screening eligibility: There was evidence that higher household income was associated with greater screening eligibility ($k = 1$) but results regarding education were mixed ($k = 2$). Screening completion/intentions: There was some evidence that patients with lower income were less likely to complete screening or have the intention to be screened (found in $k = 2$ out of $k = 3$). Stage: There was no difference in stage at diagnosis as a function of SES ($k = 1$). Mortality: High risk smokers with higher education had lower cancer-specific mortality ($k = 1$). |
| Wang 2020 | Childhood SES based on education level, socio-economic position of | Lung cancer-specific mortality | Start–2020 | 13 (8 in meta-analysis, 7 in dose-response analysis) | UK (k = 9), Norway (k = 3), Netherlands (k = 1) | 2,779,242 | Lower childhood SES was associated with higher lung cancer mortality, HR = 1.25 (95% CI, 1.10, 1.43), $P = 49\%$, $p = 0.04$, $k =$ unclear (from adjusted analysis). There was also a dose-response relationship. |

parents, and/or
childhood housing
conditions

Table 2. Information about covariate adjustment, risk of bias assessment, and methodological limitations of each review.

| First Author and Pub. Year | Are Results and Conclusions Based on Adjusted Analysis in Original Studies? | Instrument Used to Assess the Methodological Quality of Original Studies | Overall Methodological Quality of Included Studies | Main Limitations of the Review | |
|----------------------------|---|---|--|--|--|
| Afshar 2021 | Yes | Studies adjusted for a variable combination of some of the following variables: Sex, age, stage, smoking, histopathology, treatment, comorbidity, performance status. | ROBINS-E (Risk of Bias in Non-Randomized Studies Exposures) tool assessing confounding, selection of participants into the study, classification of risk of bias, the majority of the exposure, adjustment for mediators, level of missing data, measurement of the outcome, and reporting of results. | 68 of 74 articles had critical quality due to inappropriate adjustment. | Large between-study heterogeneity in the measures of SES and the methods used to identify the underlying causes of socio-economic inequalities. Frequent use of overall survival as outcome (instead of cancer-specific, which would be more useful for studying potential mediators in the context of lung cancer and considering competing risk of death). |
| Finke 2018 | Yes | The majority of studies adjusted for age, gender, and stage. Some but not all studies also for smoking and treatment. Overall, adjustment was variable. Whenever possible, subgroup analyses were performed by adjustment for smoking status, stage, and treatment. | A modified version of the Newcastle-Ottawa-Scale (NOS) that assesses the quality of a study regarding the selection and comparability of study groups and ascertainment of the outcome (cohort studies) or exposure (case-control studies) | Mean quality scores of both individual and area-based studies were overall high, between 7 and 8 out of 8 possible points. The majority of studies used data from cancer registries, and hence many studies scored high on selection and outcome, adequacy of follow-up or representativeness of study population. | Studies were very heterogeneous, not only in the use of socioeconomic measures and aggregated levels but also in reporting of survival measures and in the level of adjustment. The generalizability of results to low-income countries is limited. No meta-analysis stratified by gender or subtype of lung cancer was possible. |
| Forrest 2013 | Yes | The majority of studies adjusted for age, sex, and histology. However, it was variable and the ORs | A study quality tool, adapted from existing quality tools (SIGN 50 and STROBE) that assessed population | Quality was variable but only | Only one study measured SES on the individual level. Not all studies reported details of stage and histology— |

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|---------------------------|---|--|---|---|
| | | used in the meta-analyses were not consistently adjusted for the same covariates. | representativeness, internal validity, external validity, study reporting, confounding, and analysis (uni- or multi-variable). | studies conducting multivariable analysis (withies did not take comorbidity into account. The possibility for publication bias could not be excluded. |
| Forrest 2017 Partially | Stage: Only studies conducting multivariable analysis were included in the meta-analysis. However, the ORs used in the meta-analyses were not consistently adjusted for the same covariates. Other outcomes without meta-analysis: the presence of adjustment was variable. | A quality checklist adapted from Forrest et al. 2013 and the Aarhus checklist assessing validity and reliability of the outcome and exposure measures, analysis (adjustment and reporting), and study population. | No information on overall quality is reported. Only studies with sufficient quality were considered for meta-analysis (based on adjusted analysis). | Very few of the studies included in this current review took account of patient health status when examining time intervals. The included studies reported observational data only and use very diverse measures of socio-economic status. The meta-analysis may be underpowered to detect differences between early and late-stage presentation. The ORs used in the meta-analyses were not consistently adjusted for the same covariates. Many of the studies included in the narrative review were not of high quality. Publication bias is a possibility. |
| Mitchell 2015 Unclear | Nothing is reported in this respect. | Because included studies used methodologies that were often inapplicable to existing instruments, a method for assessing the strength of evidence of observational studies developed in previous systematic reviews was adapted, evaluating population, ascertainment, and analysis. | All studies reporting on SES were classified as "strong" (highest methodological classification). | Few evaluative studies were identified, with most researchers undertaking observational work utilizing routine data. |
| Norris 2020 No | Unadjusted ORs were used to enable inclusion of as many studies as possible in a consistent way (because not many original studies reported adjusted ORs) | A modified version of the ISPOR checklist for retrospective database studies assessing data sources, statistical results of interest, and generalizability of conclusions drawn. | Quality scores for the lung cancer studies were variable: ranging from 6 to 10 points for the biomarker studies and 6 to 8.5 for the biological and precision therapies (from a maximum of 10). | ORs were determined from raw data unadjusted for confounders. There was large heterogeneity between studies. Title and abstract screening were carried out by a single reviewer. There were only a few studies available, and most were from the US and in older patients. |

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|-----------|---|--|--|
| Sosa 2021 | All but one studies were judged as Part I “adjusting statistically for confounders”; however, it is not specified with confounders. | The National Heart, Lung, and Blood Institute Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies that assesses potential flaws in study methods or implementation that may lead to bias and lower study quality. | Five studies were judged as “good” (best category) der-related disparities were reviewed; most studies were and one as “fair” (second observational and/or secondary analysis studies; only a best). qualitative synthesis could be conducted. |
| Wang 2020 | Yes | It is not reported what factors were adjusted for. | A score system based on the Newcastle-Ottawa Scale (NOS) tool assessing representativeness of exposure arm(s), selection of the comparative arm(s), origin of exposure source, demonstration that outcome of interest was not present at start of study, studies controlling the most important factors, studies controlling the other main factors, assessment of outcome with independency, adequacy of follow-up length (to assess outcome), lost to follow-up acceptable (less than 10% and reported). |

3.1. Incidence and Mortality

We did not locate any reviews that met the inclusion criteria regarding incidence.

Wang et al. [28] investigated if childhood SES, defined as the education level or socio-economic position of parents, and/or childhood housing conditions, influenced lung cancer mortality (number of studies $k = 13$). Lower childhood SES was associated with higher lung cancer mortality, $HR = 1.25$ (95% CI, 1.10, 1.42), $p = 0.04$, $I^2 = 49\%$, $k = 10$ (from adjusted analysis, for lowest vs. highest SES). There was also evidence for a dose-response relationship. This review was still in the pre-print stage and had not been externally reviewed. It received a low confidence rating in our assessment mainly because the pre-registered protocol did not match the reported review and the risk of bias of individual studies was not considered when interpreting the results (although most studies had good scores according to the scale used (see Table 2)).

3.2. Diagnosis-Related Outcomes

Screening: Sosa et al. [17] investigated socio-economic disparities in lung cancer screening, focusing only on studies conducted in the US ($k = 6$). Annual LCS with LDCT had been recommended in the US for adults aged 55 to 80 years who are current smokers with a 30 pack-year smoking history or who are former heavy smokers who have quit within the past 15 years [29] (these criteria have been recently updated to be broader [30]). In one available study, lower household income was associated with lower screening eligibility ($k = 1$). The effects of education on screening eligibility were mixed ($k = 2$). There was some evidence that patients with lower income were less likely to complete screening or have an intention to be screened (found in $k = 2$ out of $k = 3$). However, there was no difference in stage at diagnosis as a function of SES ($k = 1$). One study also found that high risk smokers with higher education had lower cancer-specific mortality. Overall, this review shows some evidence for socio-economic inequalities in screening in the US, although the number of included studies is very limited. This review received a low confidence rating mainly because no protocol was pre-registered and the risk of bias assessment was not strongly considered when interpreting the results (although the majority of studies had good scores on the assessment used, see Table 2).

Intervals in the cancer care pathway: Forrest et al. [31] found no differences in the duration of different intervals (eight intervals in total, such as patient, GP-referral, and diagnostic interval, among others) based on socio-economic status ($k = 12$). However, very few of the studies considered the patient's health status, which is an important confounder because it can influence the time patients spend in the different healthcare intervals.

Emergency presentation: Forrest et al. [31] also investigated several proxy measures for delayed presentation such as acute presentation, emergency admission, number of times to consult, and diagnosis at death ($k = 8$). More deprived patients were more likely to present and/or be admitted as an emergency, but socio-economic inequalities were not found in the number of times to consult or in diagnosis at death.

Mitchell et al. [32] investigated what factors are related to emergency presentation defined as a diagnosis of cancer that arose during an unscheduled, emergency, or unplanned hospital admission. Higher socio-economic deprivation (as measured by area-based indices) was found to increase the likelihood of emergency presentation in all $k = 3$ studies identified. One study examined the association between annual household income and emergency presentation, but it was not significant.

As a result of the overlapping research questions, the studies identified by Mitchell et al. [32] and Forrest et al. [31] largely overlapped and reached similar conclusions. In particular, three of the four identified studies in the earlier review by Mitchell et al. were included in the later review by Forrest et al. Mitchell et al. received a low and Forrest et al. a moderate confidence rating. Overall, a yet small number of studies supports the idea that patients of lower SES are more likely to present and be admitted as an emergency.

Stage at diagnosis: Forrest et al. [31] found no evidence ($k = 23$) of socio-economic inequalities in late stage at diagnosis in the most, compared with the least, deprived groups ($OR = 1.04$, 95% CI = 0.92 to 1.19, $p = 0.53$, $I^2 = 60\%$, $k = 7$). Studies that were not suitable for meta-analysis ($k = 16$) showed the same pattern of results.

3.3. Treatment-Related Outcomes

Forrest et al. [10] investigated if SES was related to the receipt of traditional treatment (surgery, chemotherapy, radiotherapy, or unspecified treatment). Of the 46 studies they located, only one was based on an individual-level measure, whereas 45 used area-based measures of SES. Overall, lower SES was associated with lower likelihood of receiving any type of treatment: $OR = 0.79$ [95% CI 0.73 to 0.86], $p < 0.001$, $I^2 = 77\%$, $k = 26$. Regarding the different treatment modalities, patients of lower SES were less likely to undergo surgery: $OR = 0.72$ (95% CI 0.65 to 0.80), $p < 0.001$, $I^2 = 80\%$, $k = 16$ (also when controlling for histology and stage at diagnosis), chemotherapy, $OR = 0.81$ (95% CI 0.73 to 0.89), $p < 0.001$, $I^2 = 68\%$, $k = 10$, and unspecified treatment (i.e., when the article did not report the specific type of treatment), $OR = 0.78$ (95% CI 0.74 to 0.83), $p < 0.001$, $I^2 = 0$, $k = 5$. There was no association of SES with the receipt of radiotherapy, $OR = 0.99$ (95% CI 0.86 to 1.14), $p = 0.89$, $I^2 = 54\%$, $k = 7$. One limitation of the review was that not all studies reported details about stage, histology, and comorbidity, all of which can influence treatment. This review received a moderate confidence rating and was the review with the fewest methodological flaws according to the AMSTAR-2.

Norris et al. [19] investigated if SES was related to the receipt of next generation treatments, including predictive biomarker tests and biological and precision therapies, locating $k = 11$ studies on lung cancer. There was no relationship between SES and utilization of predictive biomarker tests (epidermal growth factor receptor and/or anaplastic lymphoma kinase): $OR = 0.92$ (95% CI 0.35 to 2.40), $P = 97\%$, $k = 2$ (the two studies found relationships in the opposite direction). However, lower SES was related to lower utilization of biological and precision therapies, $OR = 0.71$ (95% CI 0.51 to 1.00), $P = 95\%$, $k = 6$ (low compared to high SES). All studies identified were conducted in the US. An important limitation was that ORs were determined from raw data unadjusted for confounders. This review received a low confidence rating, mainly because of this methodological shortcoming and because the risk of bias of individual studies was not taken into account when analysing and interpreting the results.

Overall, results suggest that patients of lower SES are less likely to receive both conventional treatments such as surgery and chemotherapy and next-generation treatments such as biological and precision therapies.

3.4. Survival

Finke et al. [11] investigated socio-economic differences in lung cancer survival based on 94 studies (23 based on individual SES measures and 71 on area-based SES measures). Regarding individual-level measures, there was no effect of education level ($HR = 1.03$ [95% CI 0.96 to 1.10], ref = high education, $I^2 = 55\%$, $k = 13$) and occupations associated with lower SES did not show lower survival ($k = 3$). However, lower income was associated with lower survival ($HR = 1.13$ [95% CI 1.08 to 1.19], ref = high income, $I^2 = 0\%$, $k = 7$).

Regarding area-based measures, although meta-analysis could not be conducted the results were generally quite consistent, with lower survival among patients residing in lower SES areas, as shown by indicators of education ($k = 3$), income ($k = 19$), or a SES-index ($k = 22$).

Overall, studies were very heterogeneous, not only in the use of socioeconomic measures and aggregated levels but also in the reporting of survival measures and in the level of adjustment. Nevertheless, the range of differences between survival rates for lowest and highest SES groups was larger in studies considering area-based SES than in studies assessing individual SES. The generalizability of results to low-income countries is

limited. This review received a moderate bias rating due to several methodological shortcomings that we did not consider critical.

Finally, Afshar et al. [6] conducted a large review to investigate the factors that explained socio-economic disparities in cancer survival, locating $k = 7$ studies that provided data on lung cancer. They concluded that inequalities in lung cancer survival appear to be partly explained by the receipt of treatment and comorbidities. Results regarding the mediating role of stage at diagnosis were mixed. A limitation was that the majority of studies used overall survival as outcome instead of cancer-specific survival (controlling for other causes of death), which would be more useful for studying potential mediators in the context of lung cancer, given that there are relevant socio-economic disparities regarding multiple causes of death. This review received a moderate bias rating due to several methodological shortcomings that we did not consider critical.

4. Discussion

There is evidence of multiple and multilevel socio-economic inequalities in diverse lung cancer outcomes related to diagnosis, treatment receipt, and survival from lung cancer. Figure 3 offers a general summary of the evidence available regarding inequalities in lung cancer outcomes, including both the results from the systematic reviews that met our strict inclusion criteria and the results from other reviews discussed below that offer valuable complementary information.

No systematic reviews about the relationship between SES and lung cancer incidence met the inclusion criteria. However, we are aware of two previous reviews [9,14] that found evidence for higher risk of lung cancer among people from lower SES, regardless of the type of SES indicator used (individual or area-based). One review was published before 2009 [14] and both lacked risk of bias assessment for the individual studies [9,14]. Both reviews were, however, based on a large number of studies and considered whether individual studies adjusted for smoking. The older review considered studies from all over the world by also conducting meta-analysis, whereas the more recent review was focused on Europe. Overall, despite these differences and considering the limitations, both reviews provided evidence that lung cancer risk is higher among people from lower SES. In addition, the effect of SES on lung cancer incidence persisted, albeit diminished, after adjusting for smoking. In particular, smoking was estimated to explain 40–70% of the increased risk among people with lower SES [9,14]. The prevalence of smoking tends to be higher among the socio-economically disadvantaged [33], however, the fact that socio-economic disparities in lung cancer risk persist after accounting for smoking habits suggests that there are other contributing factors to the effect of SES on lung cancer incidence.

Regarding cancer mortality, one review associated lower SES during childhood with higher cancer mortality during adulthood [28]. This review was still in a pre-print stage and received a “low confidence” rating due to multiple flaws. However, its conclusions are supported by another rapid review [34] that located 13 studies on lung cancer, in which lower childhood SES was related to higher mortality, with this effect being attenuated after adjusting for adult SES. Overall, the available results on epidemiological indicators suggest that both childhood and adulthood socio-economic circumstances are likely to contribute to adult lung cancer risk, at least partially through cumulative exposure to smoking.

When it comes to the diagnostic process, no differences were observed between the duration of different intervals on the cancer care pathway as a function of SES [31]. However, interval duration is traditionally very diversely reported and analysed, making results difficult to summarize in a review [35]. In addition, results may be misleading if the patient’s health state is not taken into account, as it can influence the duration of the intervals (e.g., patients who present with more advanced or acute symptoms may be re-

ferred, diagnosed, and treated faster) [31]. Hence, the relationship between SES and interval duration on the lung cancer care pathway should be examined again in the future, when more and better-quality evidence is available.

Socio-economic inequalities in lung cancer outcomes

Epidemiology: Incidence and mortality

- The risk of lung cancer is 50%-80% higher among people from lower socio-economic status. Smoking is estimated to explain 40-70% of this increased risk.  
- Lower socio-economic status in childhood predicts higher cancer mortality in adulthood**, at least partially due to smoking exposure.  



Diagnosis



- People from lower socio-economic background may be less likely to participate in lung cancer screening.  
- People from lower socio-economic background are generally not diagnosed at later stages and appear not to spend more time in the different cancer care intervals. 
- However, they may be more likely to present or be admitted as an emergency.  



Treatment

- People from lower socio-economic background are less likely to receive traditional treatments such as surgery and chemotherapy. 
- They are also less likely to receive next-generation treatments such as biological and precision therapies  and stereotactic body radiotherapy. 



Survival

- People from lower socio-economic background are more likely to die within a year after diagnosis  and generally have lower survival. 
- Inequalities in survival appear to be at least partially explained by people from lower socio-economic backgrounds being less likely to receive treatment and suffering more comorbidities. 

 Reviews included in the overview  Additional reviews

Figure 3. Summary of the available evidence about socio-economic inequality in lung cancer outcomes. Circles denote articles included in the overview of systematic reviews [6,10,11,17,19,28,31,32] and stars denote additional reviews [9,12,14,16,18,34].

In a similar vein, a somewhat more solid body of evidence documented no relationship between SES and stage at diagnosis [31]. The limited role of stage was also documented in other reviews, showing that associations between SES and surgery are independent of stage at diagnosis [10] and that, in contrast to some other cancers, the effect of SES on lung cancer survival is due to differences in treatment receipt and comorbidities, but not stage at diagnosis [6].

There was evidence that people from lower SES may be less likely to undergo screening for lung cancer [17] and may be more likely to be diagnosed as an emergency [31,32].

Both findings are based on a small number of studies, mostly from the US. For instance, lung cancer screening with low dose computed tomography (LDCT) is implemented in a very small number of countries (e.g., US, South Korea, Poland), but is already underway in many other countries (e.g., Canada, UK, Germany, Italy etc.) [36]. LDCT was found to reduce lung cancer mortality by 20–24% in high-risk smokers in the National Lung Screening Trial in the US [37] and the Dutch–Belgian NELSON trial in Europe [38]. However, with the current screening criteria, it may be that people of a lower SES are less likely to be eligible for screening [16] and appear to be underrepresented in screening programs [39]. Hence, we are yet to see the full extent of effects of socio-economic and other related factors (e.g., ethnicity, rurality, etc. [40]) on lung cancer screening outcomes. For instance, SES-based differences in stage at diagnosis could emerge in areas with population screening programs if there are underlying SES-based differences in screening eligibility and utilization, something that would widen the gap in survival between people with high vs. low SES.

A large body of evidence shows that individuals from lower socio-economic backgrounds have 20–30% lower odds of receiving traditional treatments, such as surgery and chemotherapy (with ORs between 0.70–0.80) [10]. A more recent review also concluded that they also had about 30% lower odds to receive next-generation treatments, such as biological and precision therapies [19]. However, this latter review was based on a much smaller number of studies conducted in the US only and on unadjusted effect estimates. Hence, more research is needed to confirm these findings and shed light on related issues, such as the use of predictive biomarker tests. For instance, in the treatment of non-small cell lung cancer, stereotactic body radiation therapy (SBRT) is a more recent treatment that is considered better than the more conventional fractionated external beam radiation (CFRT) (e.g., higher effectiveness and lower toxicity) [18]. A recent narrative review suggests that people from lower socio-economic backgrounds are less likely to receive SBRT and are instead more likely to receive CFRT or no treatment [18].

Overall, these results regarding the access to new screenings and therapies are generally in line with the inverse equity hypothesis [41], stating that new interventions, due to their elevated cost and other issues related to access, would initially only reach and benefit the rich, and thus widen socio-economic disparities in outcomes. For instance, more economically disadvantaged patients may be less likely to receive next-generation sequencing and thus be less likely to be eligible for new precision therapy clinical trials [42]. However, it is expected that as new interventions become standard practice, they would also reach the more socio-economically disadvantaged, eventually reducing socio-economic disparities [19,41].

Finally, perhaps the most abundant evidence in this context related lower SES to lower survival from lung cancer based on 94 studies from all over the world [11]. Studies were often too diverse to summarize into a common metric, but hazard ratios were generally not higher than HR = 1.10. Lower SES is also likely associated with early lung cancer mortality (broadly defined as death after 1–12 months following diagnosis [12]). In addition, another review specifically focused on exploring the underlying mechanisms by which SES affects cancer survival and concluded that, in the case of lung cancer, these were most likely explained by differences in treatment receipt and comorbidities [6].

The diverse socio-economic inequalities observed in multiple lung cancer outcomes suggest the need for a multi-level policy approach to reduce disparities that starts from primary lung cancer prevention and extends into survivorship. For instance, interventions that effectively increase awareness of lung cancer risk factors [43] and decrease tobacco use among socio-economically disadvantaged populations [33] can reduce inequalities in cancer incidence. Recently, several areas with “most immediate need for action” in the European context have been defined to reduce inequalities in cancer outcomes [44] that are highly relevant to lung cancer, in light of the results of the current review. These include equity, with regard to (1) awareness and compliance with the European Code against Cancer (i.e., a set of cancer prevention recommendations), (2) access to cancer

screening programs, (3) reducing the time elapsed between the start of symptoms and the establishment of a cancer diagnosis, and (4) access to timely treatment and the treatment decision making process, among others.

Limitations of the current umbrella review include the perhaps very strict definition used to define a systematic review, which required that several criteria be met, among which that the search strategy is fully reported and that the individual studies are assessed in terms of risk of bias. On one hand, using such a strict definition resulted in the selection of the most robust and reproducible reviews. On the other hand, it meant that some otherwise excellent reviews which contain very useful findings were left out. To overcome this limitation, we have included such reviews in the overview of results displayed in Figure 3, which also clearly differentiates which reviews met the inclusion criteria and which did not.

None of the systematic reviews identified received a “high confidence” rating on the AMSTAR-2. We believe this is because the criteria used to assign such a rating were relatively strict and because many authors may not be aware of the importance of some methodological and reporting procedures in reviews of non-randomized observational studies. For instance, none of the reviews reported a list of the excluded studies with reasons for exclusion for each (item 7) and all but one failed to extract information regarding the funding of the original studies (item 10) and give justification for considering only non-randomized studies (item 3). Items 7 and 10 may be perceived as more relevant for reviews of clinical trials and item 3 as something self-explanatory because SES does not normally render itself to randomization. Overall, our opinion is that the reviews with a “moderate” rating have provided transparent and trustworthy synthesis of the data, whereas the findings of those with a “low” rating should be further confirmed, especially because these were also the reviews based on a relatively small number of studies. Hence, the overview is also limited by the quality and quantity of the evidence it is based on. As such, more evidence is needed in emerging areas of research such as screening and next-generation tests and treatments. Almost all of the evidence was based on high-income countries (e.g., USA, UK, other European countries). More studies are needed from middle- and lower-income countries to understand the socio-economic equalities that may exist within them.

Finally, only one of the identified reviews (Wang et al. on the effect of childhood SES on lung cancer mortality [28]) considered analysis stratified by sex, finding similar results for men and women. The rest of the reviews did not investigate to what extent the effect of SES varied among men and women, something that should be addressed in future research. The reviews on disparities in survival [6,11], conventional treatment receipt [10], and stage [31] were largely based on studies that controlled for sex in their primary analysis, so the presented results on these outcomes have been adjusted for this factor.

5. Conclusions

There are pervasive socio-economic inequalities in lung cancer incidence, mortality, and survival. These have been documented in both studies using individual-level indicators such as education, income, and/or occupation, and studies using area-level indicators such as neighbourhood deprivation indices. Compared to people with high SES, people with lower SES appear to be more likely to develop and die from lung cancer. People with lower SES also have lower cancer survival, most likely due to lower likelihood of receiving traditional and next-generation treatment, higher rates of comorbidities, and higher likelihood of being admitted as emergency. People with lower SES are generally not diagnosed at later stages, but this may change after broader implementation of lung cancer screening, as early evidence suggests that there are socio-economic inequalities in its use.

Supplementary Materials: The following supporting information can be downloaded at the Open Science Framework (OSF): <http://doi.org/10.17605/OSF.IO/TS5G8>, accessed on 13 January 2022.

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editing, D.R.-S., D.P., M.R.-B., P.F.-N., J.J.J.-M., M.-J.S.; visualization, D.R.-S. and D.P.; supervision, M.-J.S.; funding acquisition, M.-J.S. and D.P. All authors have read and agreed to the published version of the manuscript.

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Artículo 2 - Association of socioeconomic deprivation with life expectancy and all-cause mortality in Spain, 2011–2013

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Association of socioeconomic deprivation with life expectancy and all-cause mortality in Spain, 2011–2013

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Life tables summarise a population's mortality experience during a time period. Sex- and age-specific life tables are needed to compute various cancer survival measures. However, mortality rates vary according to socioeconomic status. We present sex- and age-specific life tables based on socioeconomic status at the census tract level in Spain during 2011–2013 that will allow estimating cancer relative survival estimates and life expectancy measures by socioeconomic status. Population and mortality data were obtained from the Spanish Statistical Office. Socioeconomic level was measured using the Spanish Deprivation Index by census tract. We produced sex- and age-specific life expectancies at birth by quintiles of deprivation, and life tables by census tract and province. Life expectancy at birth was higher among women than among men. Women and men in the most deprived census tracts in Spain lived 3.2 and 3.8 years less than their counterparts in the least deprived areas. A higher life expectancy in the northern regions of Spain was discovered. Life expectancy was higher in provincial capitals than in rural areas. We found a significant life expectancy gap and geographical variation by sex and socioeconomic status in Spain. The gap was more pronounced among men than among women. Understanding the association between life expectancy and socioeconomic status could help in developing appropriate public health programs. Furthermore, the life tables we produced are needed to estimate cancer specific survival measures by socioeconomic status. Therefore, they are important for cancer control in Spain.

The burden of cancer is rising globally, exerting a significant strain on populations and health systems at all income levels. Given the socio-demographic changes in Western societies, cancer control is currently one of the most complex health challenges¹. National and regional estimates of population-based cancer survival measures serve to evaluate the effectiveness of health care systems in improving cancer outcomes².

Life tables are needed to estimate the burden of cancer through several cancer survival measures using population-based cancer registry data (e.g., net survival, crude probability of death, life-years lost due to cancer, etc.)^{3,4}. Net survival is an important policy-based statistic for cancer control that reflects the probability of surviving cancer in the absence of other causes of death. It is a measure that is not influenced by changes in mortality from other causes and, therefore, provides a useful measure for tracking survival across time and comparisons between socioeconomic groups or between regions⁵. In addition to being used for the estimation of cancer survival measures, life tables are the basis for calculating life expectancy (LE)⁶. LE at birth is an important indicator that reflects social inequalities in health across the life course, influenced by age, sex, geographical region, and socioeconomic status (SES). However, there are no available estimates of LE at birth by SES in Spain meaning that important cancer specific survival measures by SES for cancer control are not yet estimated in Spain.

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Despite efforts worldwide and in Europe, social inequalities in cancer survival persist⁷. Social inequalities in cancer outcomes have an economic impact on health care costs⁸. Therefore, identifying and characterising socioeconomic and geographic disparities in LE can help in evaluating socioeconomic disparities in cancer survival. Identifying LE and cancer survival measures helps optimise and redistribute healthcare services more equitably. However, to estimate these cancer survival measures by SES for a specific geographical area, we need to incorporate the overall area mortality rate obtained from national or regional life tables⁹. Furthermore, life tables by socioeconomic status have not been computed in Spain yet highlighting the relevance of our work for cancer research, control, and social inequalities in health. We hypothesize that SES is associated with LE at birth, i.e., people living in more affluent areas have longer LE than people living in the most deprived areas of Spain.

Therefore, we aimed to construct life tables by sex, age, and SES at the census tract level and by provinces for the 2011–2013 period in Spain and to produce comparative estimates of LE by sex, age, region, and SES in Spain.

Methods

Study design, participants, data, and setting. We conducted a population-based, multilevel study to derive LE at birth by SES in Spain. Population and mortality data were drawn from the Spanish Statistical Office for the 2011–2013 period using census tract level, age, calendar year, and sex (Spanish Statistical Office data cession agreement number 67/2020). LE at birth for the 2011–2013 period is essential for cancer control and establishing temporal comparisons (i.e., trends) over time when new information from the national census will be made publicly available in Spain.

We used the layer of census tracts of the Spanish Census in 2011, with 35,960 census tracts. The mean area of the census tracts is 14.04 km² (5.42 mi²), and the mean population is 1,311 inhabitants for census tract, with the closest equivalent in the US geographic levels being the census block group¹⁰. To measure deprivation in each census tract, we used the Spanish Deprivation Index (SDI)¹¹ created by principal component analysis¹² using data from the Spanish 2011 census conducted by the Spanish Statistical Office (https://www.ine.es/dyngs/INEbase/en/categoría.htm?c=Estadística_Pcid=1254735572981).

The SDI includes information from six indicators mainly related to employment and education: percentage of manual workers (employed or unemployed), percentage of occasional workers (employed or unemployed), percentage of the population with insufficient education (i.e., less than 8 years of secondary studies), and percentage of main homes without internet access¹¹. While the index has no direct information about income, we discovered in a previous study that the SDI and average income per person are associated at the census tract level¹³. We used the SDI divided in quintiles (Q), where Q5 represents the 20% of census tracts which are the most deprived areas (lowest SES) and Q1 the 20% of census tracts which are the least deprived areas (highest SES).

The Internal Review Board of the Andalusian School of Public Health (CP17/00206), Granada Provincial Intern Research Review Committee and the Biomedical Ethics Committee of the Department of Health of the Andalusian Regional Government (study 0072-N-18) approved the study protocol. The study conforms to the principles embodied in the Declaration of Helsinki.

Statistical analysis. We performed a descriptive analysis, where we first computed the crude mortality rates per 100,000 people for the overall period and by quintiles of deprivation, categories of age, and sex in Spain. To compute mortality rates, we used the total population at risk for the analysed period.

The counts of deaths and population produced by the Spanish Statistical Office were available only for five-year age groups from 0 to > 85 years (i.e. abridged). Therefore, we used a modified modelling approach described elsewhere¹⁴ to estimate the smoothed mortality rates using a flexible Poisson multivariable mixed-effects model¹⁵. Death counts were modelled in the generalised linear model framework, considering a Poisson error, using restricted cubic splines to capture the smoothed effect of age, and including the at-risk population as an offset¹⁶. Models were stratified according to sex. The covariates considered in the model were restricted cubic splines of age (using the mid-age of each age group), quintile of the SDI, interaction between SDI and age, and random intercept for the census tracts. The model specification is given by:

$$\ln(\text{cases}_{\text{age}, \text{SDI}} / \text{population}_{\text{age}, \text{SDI}})_j = \beta_0 + f_1(\text{age}) + \sum_{i=2}^5 \beta_i \times \text{Quintile SDI}_i + f_2(\text{quintile SDI}_i \times \text{age}) + Q_j \quad (1)$$

where Q_j is the random intercept for the j census tract, and f₁ and f₂ represent the restricted cubic splines for age and the interaction between age and the quintiles of SDI, respectively.

We used a data-adaptive cross-validated approach to identify the best position and number of knots for the mean-centred age of 60 years. The knot positions were fixed at ages 2, 12, 22, 32, 42, 52, 67, and 82 based on the lowest cross-validated mean absolute error of a set of models with different knot positions¹⁷.

We included the census tract as a random intercept [Q_j in (Eq. 1)] to account for the non-spatial variability and improve the model fit, given that the random effects approach penalised smoothing splines, which reduced overfitting¹⁸. From the fitted model, we predicted the smoothed mortality rates accounting for the random intercept by age group and quintile of deprivation, stratified by sex. We derived LE for people ≥ 75 years old by census tracts from the life tables and presented it in choropleth maps. LE quintiles were computed by dividing the census tracts in five groups, where Q1 represents the 20% of census tracts which have the lowest LE, and Q5 the 20% of census tracts which have the highest LE. Furthermore, we computed the LEs at birth by province, by weighting the LE for all the census tracts of the province with the population size of each census tract.

To assess the goodness-of-fit of the model, we compared the predicted and observed mortality rates. We derived 95% confidence intervals for the mortality rates using the Delta method¹⁹.

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| Year | Quintile of SDI | Deaths | Population | Mortality rate per 10^5 people (95% CI) | SMR (95% CI) |
|----------------|-----------------|--------|------------|---|------------------|
| Males | | | | | |
| 2011 | Q1 | 35,217 | 5,256,845 | 6.69 (6.63–6.77) | Ref |
| | Q2 | 39,405 | 5,073,220 | 7.77 (7.69–7.84) | 1.05 (1.03–1.08) |
| | Q3 | 41,134 | 4,759,007 | 8.64 (8.56–8.72) | 1.09 (1.07–1.11) |
| | Q4 | 39,745 | 4,270,710 | 9.31 (9.21–9.40) | 1.10 (1.08–1.12) |
| | Q5 | 39,523 | 3,921,491 | 10.08 (9.98–10.18) | 1.17 (1.15–1.19) |
| 2012 | Q1 | 36,126 | 5,288,462 | 6.83 (6.76–6.90) | Ref |
| | Q2 | 40,656 | 5,075,266 | 8.01 (7.93–8.08) | 1.06 (1.04–1.08) |
| | Q3 | 42,394 | 4,750,182 | 8.92 (8.84–9.01) | 1.10 (1.08–1.12) |
| | Q4 | 41,073 | 4,254,020 | 9.65 (9.56–9.75) | 1.12 (1.10–1.14) |
| | Q5 | 40,949 | 3,888,492 | 10.53 (10.43–10.63) | 1.20 (1.18–1.22) |
| 2013 | Q1 | 35,551 | 5,272,262 | 6.74 (6.73–6.81) | Ref |
| | Q2 | 39,766 | 5,039,926 | 7.89 (7.81–7.97) | 1.06 (1.05–1.08) |
| | Q3 | 40,643 | 4,703,703 | 8.64 (8.56–8.75) | 1.08 (1.07–1.10) |
| | Q4 | 39,752 | 4,194,731 | 9.48 (9.38–9.57) | 1.12 (1.10–1.14) |
| | Q5 | 39,314 | 3,832,194 | 10.26 (10.16–10.36) | 1.19 (1.17–1.21) |
| Females | | | | | |
| 2011 | Q1 | 38,283 | 5,657,980 | 6.77 (6.69–6.83) | Ref |
| | Q2 | 37,608 | 5,270,843 | 7.14 (7.06–7.21) | 0.98 (0.96–0.99) |
| | Q3 | 37,515 | 4,853,180 | 7.13 (7.06–7.21) | 0.99 (0.98–1.00) |
| | Q4 | 35,979 | 4,277,989 | 8.41 (8.32–8.50) | 1.01 (0.99–1.03) |
| | Q5 | 34,734 | 3,845,162 | 9.03 (8.94–9.13) | 1.06 (1.04–1.07) |
| 2012 | Q1 | 39,696 | 5,699,851 | 6.96 (6.90–7.03) | Ref |
| | Q2 | 39,340 | 5,286,365 | 7.44 (7.37–7.52) | 0.99 (0.98–1.00) |
| | Q3 | 39,459 | 4,854,909 | 8.13 (8.04–8.86) | 1.01 (0.99–1.03) |
| | Q4 | 37,451 | 4,268,555 | 8.77 (8.68–8.86) | 1.02 (1.01–1.04) |
| | Q5 | 37,020 | 3,815,310 | 9.70 (9.60–9.80) | 1.10 (1.08–1.12) |
| 2013 | Q1 | 38,846 | 5,691,572 | 6.83 (6.76–6.89) | Ref |
| | Q2 | 38,137 | 5,266,307 | 7.24 (7.20–7.31) | 0.98 (0.97–0.99) |
| | Q3 | 38,004 | 4,824,427 | 7.88 (7.79–7.96) | 1.00 (0.98–1.01) |
| | Q4 | 36,221 | 4,224,892 | 8.57 (8.48–8.66) | 1.02 (1.00–1.04) |
| | Q5 | 35,242 | 3,772,367 | 9.34 (9.25–9.44) | 1.08 (1.06–1.10) |

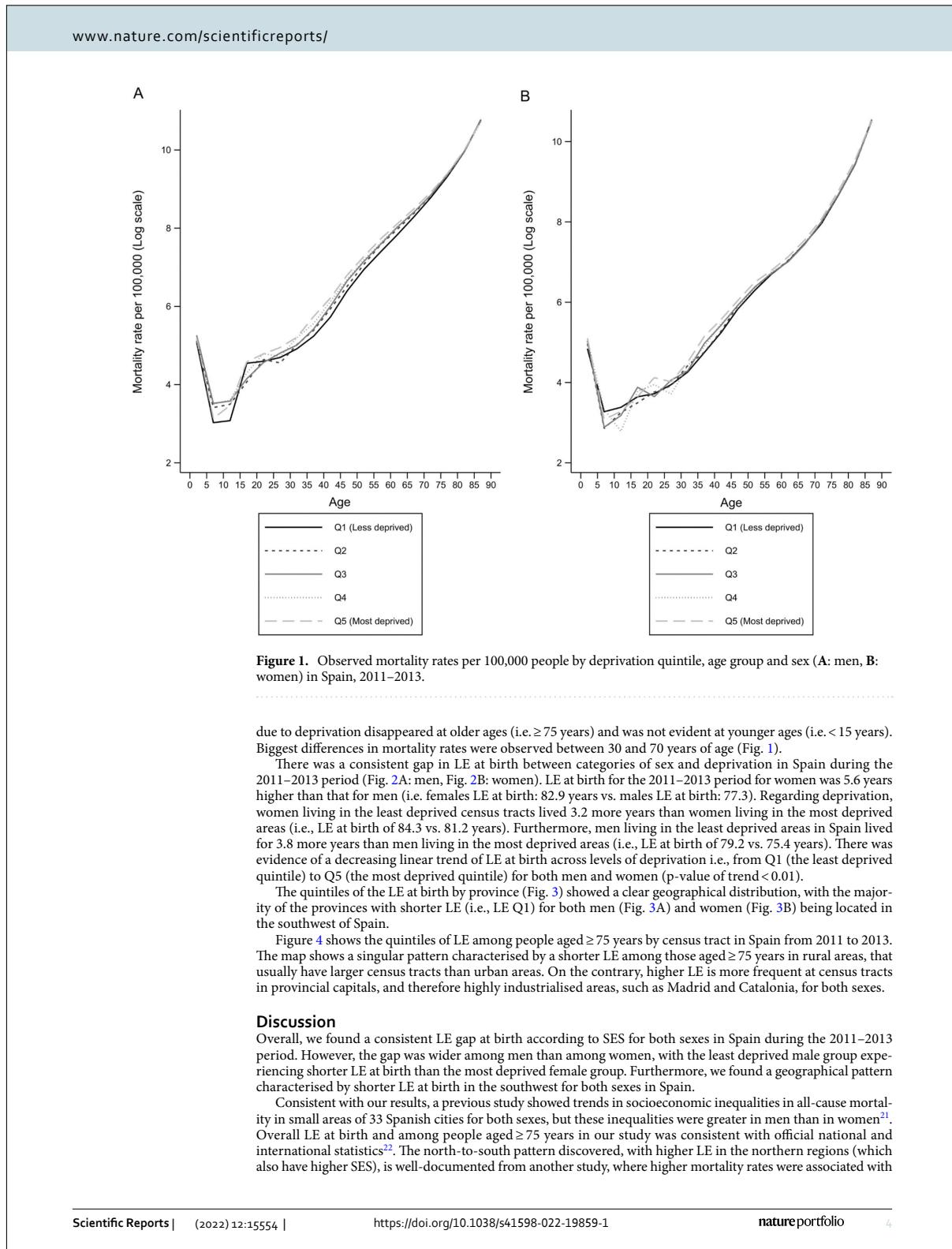
Table 1. Deaths, population, mortality rate, and standardized mortality rate with 95% confidence interval by sex, year and deprivation quintiles in Spain between 2011 to 2013. SDI Spanish Deprivation Index, Q deprivation quintiles, CI confidence interval, SMR standardized mortality rate (indirect method).

We used Stata v.16.1 (StataCorp, College Station, Texas, USA) and R v.4.1.0 (R Foundation for Statistical Computing, Vienna, Austria) for statistical analysis and mapping. The syntax files for the computation of the life tables and the derived life tables are available on GitHub (https://github.com/migariane/Spanish_LifeTables_ByDeprivation).

Ethics approval and consent to participate. The Internal Review Board of the Andalusian School of Public Health (CP17/00206), Granada Provincial Intern Research Review Committee and the Biomedical Ethics Committee of the Department of Health of the Andalusian Regional Government (study 0072-N-18) approved the study protocol. The study conforms to the principles embodied in the Declaration of Helsinki.

Results

Overall, the mortality rates were higher among men than among women and also higher among people living in the most deprived areas of Spain (Table 1). Mortality rates remained stable for men and women over the 2011–2013 period (i.e. p-value of trend > 0.05). Standardised mortality rates using the indirect method¹⁰ were approximately 20% and 10% higher among men and women living in the most deprived areas, respectively, than among those living in the least deprived areas. The observed mortality rates over the 2011–2013 period in Spain by age group and quintiles of deprivation stratified by sex showed a u-shape with higher mortality rates at the extremes of the age distribution (Fig. 1). Supplementary Fig. 1 shows the goodness-of-fit of the model. The concordance of the observed vs. fitted mortality rates by age and quintiles of deprivation was good among all quintiles for > 20 years, with small discrepancies at earlier ages. Overall, the mortality rates among people living in the most deprived areas were higher among those aged > 15 years for both men and women. The mortality gap



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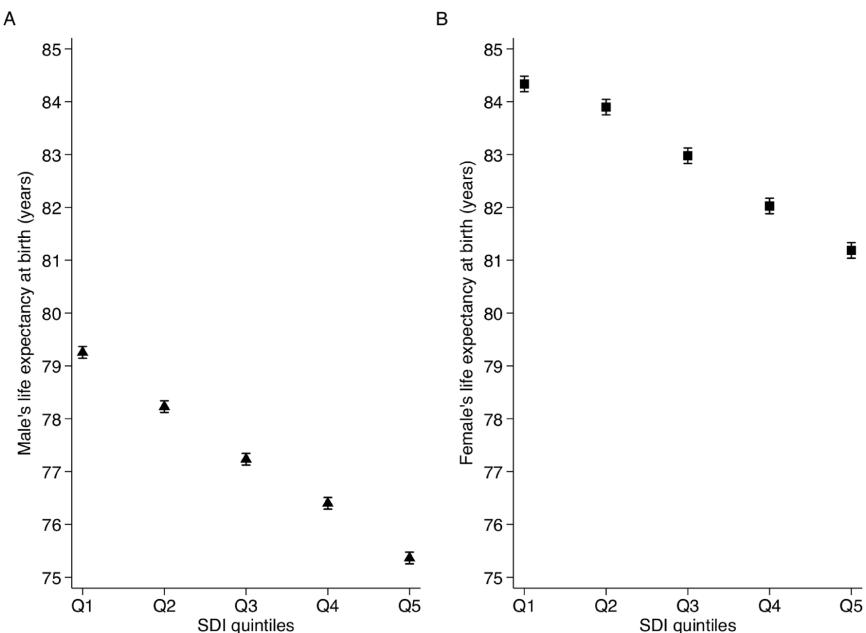


Figure 2. Life expectancy at birth (in years) by quintiles of deprivation and sex (A: men, B: women) in Spain, 2011–2013.

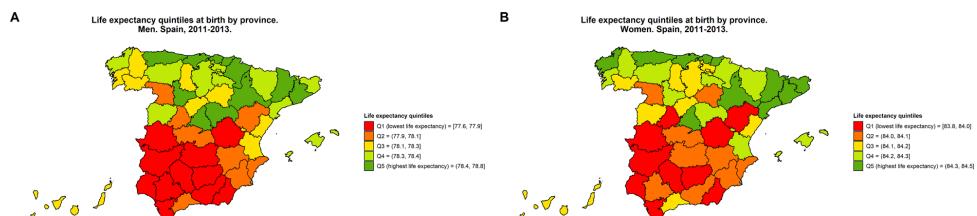


Figure 3. Life expectancy quintiles at birth by province and sex (A: men, B: women) in Spain, 2011–2013.

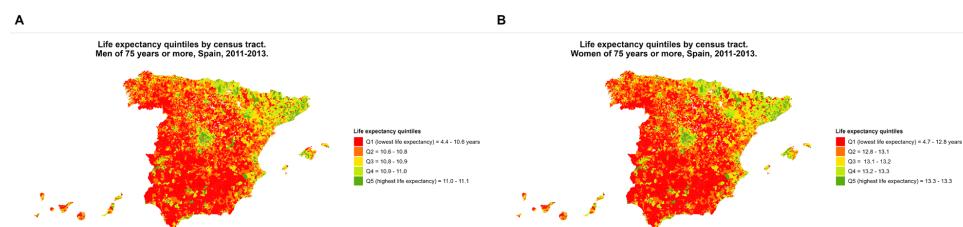


Figure 4. Life expectancy quintiles among people aged ≥ 75 years old by census tract and sex (A: men, B: women) in Spain, 2011–2013.

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particular geographical areas in Spain²³. Furthermore, our results on LE at birth by deprivation are consistent with those of other European studies²⁴. In the UK, LE at birth in 2005 presented a similar pattern, with the highest LE in the most affluent groups compared to the most deprived group, with a gap between 2.7 and 5.0 years for males and between 2.5 and 3.6 years for females²⁵. Overall, differences in LE are seen by deprivation and by region, and the regions with higher LE are also the least deprived²⁵. Similar to the geographical pattern found in Spain, a regional pattern characterised by a clear north–south gradient was found in the UK, with deprivation explaining most of the geographical variation in LE²⁵. A similar pattern was found in Portugal, where LE at birth for the 2010–2012 period was higher among the least deprived people²⁶. However, differences between the most and least deprived people were about 2.0 years higher for men and 1.0 year higher for women living in the least deprived areas of Portugal²⁶. Consistent with the findings in both Spain and the UK, LE differences progressively disappeared with increasing age in Portugal²⁶. Similar findings related to the association between shorter LE and lower income or education have been reported in other European countries, including Norway, Denmark, and Belgium^{27–29}.

In the USA and Canada, there is evidence supporting higher LE among people with higher income between 2002 to 2014, and geographical variation in LE was correlated with the characteristics of local areas in terms of health behaviour^{30,31}.

Strengths. Our study provided evidence of an LE gap between socioeconomic groups. Furthermore, the results of the study are consistent with those of other international and European studies regarding LE by deprivation. However, our study provides more and updated evidence regarding the presence of an LE gap by sex and region. To the best of our knowledge, this is the first study to assess LE at birth by age, sex, and SES in Spain. Our findings are relevant and important for the development of public health policies tackling social inequalities in health targeting the LE gap by socioeconomic status (i.e., people from more affluent regions live longer than people living in the most deprived areas). Furthermore, the life tables by province we have produced and made freely available on the GitHub repository are essential for the computation of cancer-specific survival estimates adjusted for SES. The use of the life tables in population-based cancer research can help foster novel evidence on cancer survival inequalities by SES in Spain.

Limitations. In our study, the SDI we referred to was of 2011, while mortality was measured in the 2011–2013 period. This is because the SDI is based on the national census data of Spain, which are generated every 10 years. However, it is the first time LE by SES has been computed and the life tables by age, sex, and SES that we produced will serve as a baseline reference for monitoring trends during the coming years and when the new Spanish census result are made available. We argue that the effect of deprivation on mortality will be consistent over time, but trends and changes over time must be monitored. Furthermore, the abridged nature of the data (i.e., aggregated data on age) reduces the possibility of identifying mortality differences across age groups. However, we attempted to accommodate this using a flexible modelling framework.

Another limitation was the layer of census tracts undergoing continuous changes over time. However, for our analysis, we used the fixed layer of census tracts of the National Census of 2011 (1st November 2011), which was the same as that used for the SDI, except for mortality and population data (i.e., the mortality data used the most up-to-date census tract layer at the date of each death and the population data used the census tract layer on 1st January of each year). In sensitivity analysis, the linkage results between population figures, mortality data, and SDI are shown in Supplementary Table 1. Overall, the unlinked deaths (mortality–population link) were around 1.7%, with the average number of deaths lost per year being 6567 out of 391,913 (Supplementary Table 1). The unlinked census tracts for the population–SDI link were below 0.6% for all years, with an average of 90 census tracts lost for each sex and year out of an average of 36,003 census tracts per sex and year (Supplementary Table 2). Finally, we assumed that the census tract of residence at death was the same throughout the life of a person.

Conclusions

In summary, we found an important LE gap according to sex and SES in Spain during the 2011–2013 period. The LE gap was more pronounced among men than among women and less pronounced among people aged < 75 years. Understanding the factors explaining the association between LE and SES could be helpful in the development of appropriate public health programs. The generated life tables, made available for researchers on the GitHub repository: https://github.com/migariane/Spanish_LifeTablesByDeprivation, are an essential statistical tool for estimating the net cancer-specific survival by SES, a useful indicator for detecting socioeconomic inequalities in cancer survival.

Data availability

The data that support the findings of this study are available from the Spanish Statistical Office (INE). The syntax files for the computation of the life tables and the derived life tables are available on GitHub (https://github.com/migariane/Spanish_LifeTablesByDeprivation).

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Disclaimer

This article presents independent research. The views expressed are those of the authors and not necessarily those of the Carlos III Institute of Health.

Author contributions

M.A.L.F. and B.R. designed this study. D.R.S. and M.A.L.F. analysed the data and wrote the first draft of the manuscript. All authors contributed to data generation and curation, reviewed the study results, and drafted the different versions of the manuscript.

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Competing interests

The authors declare no competing interests.

Additional information

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Artículo 3 - Lung, Breast and Colorectal Cancer Incidence by Socioeconomic Status in Spain: A Population-Based Multilevel Study

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Article

Lung, Breast and Colorectal Cancer Incidence by Socioeconomic Status in Spain: A Population-Based Multilevel Study

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Simple Summary: Despite political efforts across the world and Europe, social inequalities in cancer incidence are persistent. We studied the association between socioeconomic status (SES) and cancer incidence in nine Spanish provinces. Lower SES was associated with an increased risk of lung cancer among males. Higher SES was associated with an increased risk of breast cancer among females in Spain. Understanding the reasons behind the association between cancer incidence and SES could help develop appropriate public health programs to promote health and reduce socioeconomic inequalities in cancer incidence in Spain.

Abstract: Socioeconomic inequalities in cancer incidence are not well documented in southern Europe. We aim to study the association between socioeconomic status (SES) and colorectal, lung, and breast cancer incidence in Spain. We conducted a multilevel study using data from Spanish population-based cancer registries, including incident cases diagnosed for the period 2010–2013 in nine Spanish provinces. We used Poisson mixed-effects models, including the census tract as a random intercept, to derive cancer incidence rate ratios by SES, adjusted for age and calendar year. Male adults with the lowest SES, compared to those with the highest SES, showed weak evidence of being at increased risk of lung cancer (risk ratio (RR): 1.18, 95% CI: 0.94–1.46) but showed moderate evidence of being

at reduced risk of colorectal cancer (RR: 0.84, 95% CI: 0.74–0.97). Female adults with the lowest SES, compared to those with the highest SES, showed strong evidence of lower breast cancer incidence with 24% decreased risk (RR: 0.76, 95% CI: 0.68–0.85). Among females, we did not find evidence of an association between SES and lung or colorectal cancer. The associations found between SES and cancer incidence in Spain are consistent with those obtained in other European countries.

Keywords: socioeconomic inequalities; colorectal cancer; lung cancer; breast cancer; epidemiology; population-based study

1. Introduction

The burden of cancer is rising globally, exerting a significant strain on populations and health systems at all income levels. Given the sociodemographic change in Western societies, cancer control will be one of the most complex health challenges in the future [1]. Estimates of population-based cancer incidence serve to evaluate cancer's burden on health systems worldwide [2]. Despite political efforts across the world and Europe, social inequalities in cancer incidence are a persistent problem [3]. Social inequalities in cancer outcomes have an economic impact on healthcare costs [4]. Thus, identifying and characterizing socioeconomic and geographic disparities in cancer outcomes helps optimize and redistribute healthcare services in a more equitable fashion.

In northern Europe, there is a long-standing tradition of measuring deprivation in small geographical areas but not in Spain [5]. Recently, a standardized measure of socioeconomic deprivation covering Spain's whole territory has been developed using the national census data from 2011, namely, the Spanish Deprivation Index (SDI). The index allows one to characterize and compare socioeconomic inequalities in cancer outcomes as a function of census tracts [6].

Using this newly developed index, we aim to study the association between socioeconomic inequalities and cancer incidence for three anatomical sites from the European High Resolution Studies [7] (i.e., colorectal, lung, and breast cancers) in Spain. Furthermore, we aim to investigate how cancer incidence varies geographically in small areas after accounting for age and the SDI in Spain during the period 2010–2013.

2. Materials and Methods

2.1. Study Design, Participants, Data, and Setting

We developed a population-based multilevel study. Data were drawn from nine Spanish population-based cancer registries (Albacete, Bizkaia, Castellón, Cuenca, Girona, Gipuzkoa, Granada, Navarra, and Tarragona) that participated in the European High Resolution Studies (TRANSCAN-HIGHCARE project within ERA-Net) [7]. Supplementary Figure S1 shows the location, within peninsular Spain, of the nine provinces of the study. Colorectal, lung, and breast cancer cases >18 years and diagnosed during the period 2010–2013 by census tract level, including their age, sex, and year of diagnosis, were included in the study. Case codes were C18–C21 with malignant behavior (/3) for colorectal, C34.0–C34.9 with malignant behavior (/3) for lung, and C50.0–C50.9 with malignant behavior (/3) or *in situ* (/2) for breast cancer among females according to the topography code of the International Classification of Diseases for Oncology, 3rd Edition [8]. Colorectal cancer data were used in a previous work to assess socioeconomic inequalities (measured with SDI) on survival in Spain [9].

Population-based figures broken down by census tract level, age, calendar year, and sex were obtained from the Spanish Statistical Office. The SDI was created by Duque et al. [6] using data from the Spanish 2011 census conducted by the Spanish National Statistics Institute. The index includes information from six indicators mainly related to employment and education: percentage of manual workers (employed or unemployed), percentage of occasional workers (employed or unemployed), percentage of the population

with insufficient education, and percentage of main homes without internet access [6]. The index has no direct information about income, but in the sensitivity analysis, we found a direct association between SDI and average income per census tract [10] (Supplementary Figure S2). We used the SDI divided in quintiles (Q), where Q5 represents the most deprived areas and Q1 the least deprived areas.

The internal review board of the Andalusian School of Public Health (CP17/00206) and the biomedical ethics committee of the Department of Health of the Andalusian Regional Government (study 0072-N-18) approved the study protocol.

2.2. Statistical Analysis

In the descriptive analysis, we first estimated the crude rates per 100,000 people for the overall period and by the quintiles of deprivation, categories of age, and sex. To compute the incidence rates, we used the total population at risk for the analyzed period. Afterward, we computed univariable- and multivariable-adjusted rate ratios using a Poisson mixed-effects model [11]. Models were stratified by sex. We added one variable at a time to control for confounding and used robust standard errors to account for overdispersion [12]. The final model was adjusted for SDI quintile, age in years, and calendar year. The model specification was given by

$$\ln(\text{cases}/\text{population}) = \beta_0 + \beta_1 \times (\text{Quintile SDI}) + \beta_2 \times (\text{Age}) + \beta_3 \times (\text{Calendar year}) + Q \quad (1)$$

where Q is the random intercept for census tracts.

We included the census tract as a random intercept (Q in (1)) to account for spatial heterogeneity. From the models, we derived the Empirical Bayesian Estimate to identify patterns of non-random variation in cancer incidence in Spain [13]. Using the posterior Empirical Bayesian prediction, we mapped the age- and SES-standardized cancer incidence smoothed rates adjusted for the SDI by census tract in Spain for colorectal, lung, and breast cancers.

We assessed different model specifications in the sensitivity analysis, including the non-linearity effect of age using restricted cubic splines. Furthermore, we assessed the consistency of the reported cancer incidence rates by calendar year and cancer registry with published evidence in official statistical sources [14].

We used Stata v.16.1 (StataCorp, College Station, TX, USA) [15] and R v.4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) [16] for statistical analysis.

3. Results

Figure 1 shows the SDI quintiles' spatial distribution in 2011 by census tract for the nine Spanish provinces under study. Overall, there was a north–south pattern with the highest deprivation in the southern provinces (Granada, Albacete, and Cuenca) compared to those in the north of Spain (Bizkaia, Gipuzkoa, Girona, Navarra, and Tarragona). The province of Castellón showed an intermediate pattern between the northern and southern provinces. Supplementary Figure S3 shows the spatial distribution of the quintiles of SDI in the provinces' capitals.

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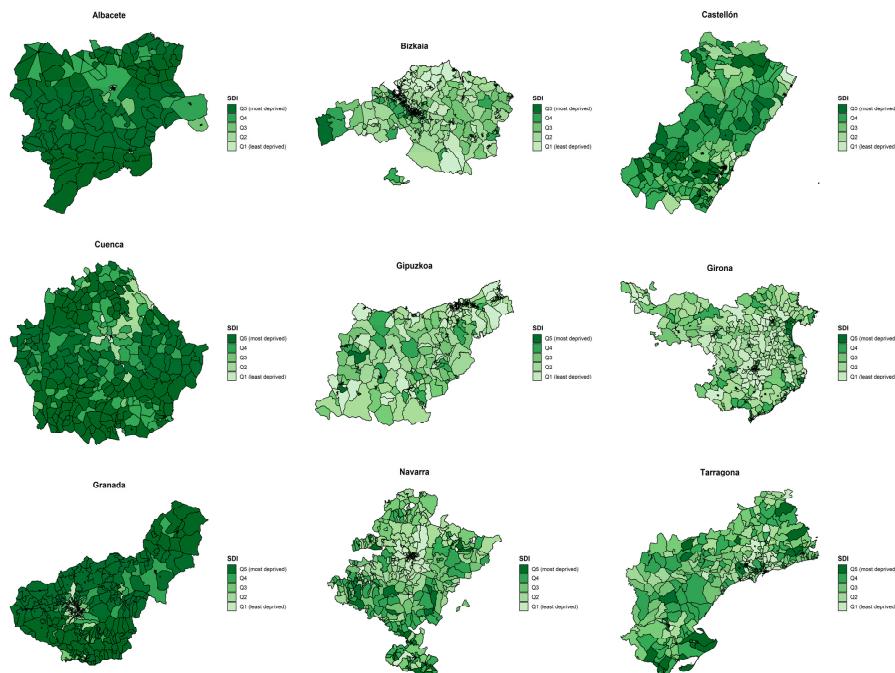


Figure 1. Quintiles of the Spanish Deprivation Index (SDI) by census tract in the nine Spanish provinces under study, 2011.

Table 1 shows the total number of cancer cases, the population at risk, and the observed incidence rates per 100,000 people during the period 2010–2013 by cancer site, sex, quintiles of deprivation, and age groups.

Table 1. Cancer incidence, population at risk, incidence rate per 100,000 people, and *p*-value for trend by sex, deprivation, and age groups in Spain for the period 2010–2013.

| Variables | Cases | Population at risk | Colorectal Cancer | | | Cases | Population at risk | Incidence rate * (95%CI) | <i>p</i> -value for trend |
|-------------------------------|-------|--------------------|---------------------|--------|-------|-------|--------------------|--------------------------|---------------------------|
| | | | Females | | Males | | | | |
| Overall rate period 2010–2013 | 1457 | 3,088,569 | 47.2 (44.8–49.7) | | | 2366 | 3,058,549 | 77.4 (74.3–80.5) | |
| Quintiles of SDI | | | | 0.031 | | | | | 0.288 |
| Q1 | 306 | 710,049 | 43.1 (38.4–48.2) | | | 502 | 666,960 | 75.2 (68.8–82.2) | |
| Q2 | 300 | 685,582 | 43.8 (39.0–49.0) | | | 504 | 669,303 | 75.3 (68.9–82.2) | |
| Q3 | 341 | 676,128 | 50.4 (45.2–56.1) | | | 500 | 673,987 | 74.2 (67.8–81.0) | |
| Q4 | 273 | 556,068 | 49.1 (43.4–55.3) | | | 497 | 567,003 | 87.7 (80.1–95.7) | |
| Q5 | 237 | 460,742 | 51.4 (45.1–58.4) | | | 363 | 481,296 | 75.4 (67.8–83.6) | |
| Age groups | | | | <0.001 | | | | | <0.001 |
| <50 | 91 | 1,913,857 | 4.8 (38.3–58.4) | | | 103 | 2,034,317 | 5.1 (4.1–6.1) | |
| 50–54 | 89 | 209,507 | 42.5 (34.1–52.3) | | | 110 | 215,299 | 51.1 (42.0–61.6) | |
| 55–59 | 123 | 173,809 | 70.8 (58.8–84.4) | | | 210 | 172,994 | 121.4 (105.5–139.0) | |
| 60–64 | 131 | 161,485 | 81.1 (67.8–96.3) | | | 280 | 155,412 | 180.2 (159.7–202.6) | |
| 65–69 | 183 | 145,714 | 125.6 (108.1–145.2) | | | 328 | 132,958 | 246.7 (220.7–274.9) | |
| 70–74 | 161 | 129,505 | 124.3 (105.9–145.1) | | | 337 | 109,816 | 306.9 (275.0–341.5) | |
| 75–79 | 236 | 137,047 | 172.2 (150.9–195.7) | | | 416 | 108,811 | 382.3 (346.5–420.9) | |
| 80–84 | 240 | 112,979 | 212.4 (186.4–241.1) | | | 354 | 77,129 | 459.0 (412.4–509.4) | |
| ≥85 | 203 | 104,666 | 194.0 (168.2–222.5) | | | 228 | 51,813 | 440.0 (384.8–501.0) | |

Table 1. Cont.

| Lung Cancer | | | | | | | | |
|-------------------------------|-------|--------------------|--|----------------------|-------|--------------------|--------------------------------------|----------------------|
| Variables | Cases | Population at risk | Females Incidence rate * (95%CI) | p-value for trend | Cases | Population at risk | Males Incidence rate * (95%CI) | p-value for trend |
| Overall rate period 2011–2012 | 180 | 1,309,540 | 13.8 (11.8–15.9) | | 887 | 1,294,591 | 68.5 (64.1–73.2) | |
| Quintiles of SDI | | | | 0.555 | | | | 0.004 |
| Q1 | 39 | 231,526 | 16.8 (12.0–23.0) | | 125 | 211,780 | 59.0 (49.1–70.3) | |
| Q2 | 21 | 230,603 | 9.1 (5.6–13.9) | | 144 | 225,239 | 63.9 (53.9–75.3) | |
| Q3 | 47 | 272,080 | 17.3 (12.7–23.0) | | 171 | 270,082 | 63.6 (54.2–73.6) | |
| Q4 | 36 | 308,654 | 11.7 (8.2–16.2) | | 211 | 311,269 | 67.8 (59.0–77.6) | |
| Q5 | 37 | 266,677 | 13.9 (9.8–19.1) | | 236 | 276,221 | 85.4 (74.9–97.1) | |
| Age groups | | | | <0.001 | | | | <0.001 |
| <50 | 23 | 843,733 | 2.7 (1.7–4.1) | | 36 | 890,011 | 4.0 (2.8–5.6) | |
| 50–54 | 34 | 88,734 | 38.3 (26.5–53.5) | | 50 | 88,958 | 56.2 (41.7–74.1) | |
| 55–59 | 21 | 71,940 | 29.2 (18.1–44.6) | | 90 | 71,123 | 126.5 (101.8–155.5) | |
| 60–64 | 26 | 65,445 | 39.7 (26.0–58.2) | | 99 | 61,409 | 161.2 (131.0–196.3) | |
| 65–69 | 12 | 57,708 | 20.8 (10.7–36.3) | | 133 | 53,024 | 250.8 (210.0–297.3) | |
| 70–74 | 7 | 50,656 | 13.8 (5.6–28.5) | | 138 | 42,560 | 324.3 (272.4–383.1) | |
| 75–79 | 23 | 53,693 | 42.8 (27.2–64.3) | | 163 | 41,764 | 390.3 (332.7–455.0) | |
| 80–84 | 17 | 41,883 | 40.6 (23.6–65.0) | | 122 | 27,786 | 439.1 (364.6–524.3) | |
| ≥85 | 17 | 35,748 | 47.6 (27.7–76.1) | | 56 | 17,956 | 311.9 (235.6–405.0) | |
| Breast Cancer—Females | | | | | | | | |
| Variables | Cases | Population at risk | Incidence rate * (95%CI) | p-value for trend | | | | |
| Overall rate period 2010–2013 | 3157 | 2,902,468 | 108.8 (105.0–112.6) | | | | | |
| Quintiles of deprivation | | | | <0.001 | | | | |
| Q1 | 721 | 567,481 | 127.1 (118.0–136.7) | | | | | |
| Q2 | 631 | 558,370 | 113.0 (104.4–122.2) | | | | | |
| Q3 | 571 | 553,979 | 103.1 (94.8–111.9) | | | | | |
| Q4 | 629 | 608,179 | 103.4 (95.5–111.8) | | | | | |
| Q5 | 605 | 614,459 | 98.5 (90.8–106.6) | | | | | |
| Age groups | | | | <0.001 | | | | |
| <50 | 912 | 1,839,937 | 49.6 (46.4–52.9) | | | | | |
| 50–54 | 393 | 193,301 | 203.3 (183.7–224.4) | | | | | |
| 55–59 | 332 | 165,866 | 200.2 (179.2–222.9) | | | | | |
| 60–64 | 350 | 153,247 | 228.4 (205.1–253.6) | | | | | |
| 65–69 | 323 | 133,590 | 241.8 (216.1–269.6) | | | | | |
| 70–74 | 208 | 112,291 | 185.2 (160.9–212.2) | | | | | |
| 75–79 | 263 | 117,201 | 224.4 (198.1–253.2) | | | | | |
| 80–84 | 197 | 95,765 | 205.7 (178.0–236.5) | | | | | |
| ≥85 | 179 | 91,270 | 196.1 (168.4–227.1) | | | | | |

* Per 100,000 people.

There were 3823 colorectal cancer cases and 6,147,118 people at risk in seven Spanish provinces during the period 2010–2013. Males showed a higher crude rate than females (77.4 per 100,000 males vs. 47.2 per 100,000 females). The crude incidence rate increased with age for both males and females, and, with quintiles of deprivation, only for females. Females with colorectal cancer living in the most deprived areas (i.e., Q5) showed 51.4 cases per 100,000 vs. 43.1 cases per 100,000 among females living in the least deprived areas (i.e., Q1).

There were 1067 lung cancer cases and 2,604,131 people at risk in two Spanish provinces during 2011–2012. Lung cancer risk increased with age for both males and females and with quintiles of deprivation only among males. Males with lung cancer living in the most deprived areas (i.e., Q5) showed a rate of 85.4 cases per 100,000 vs. 59.0 cases per 100,000 among males living in the least deprived areas (i.e., Q1).

There were 3157 breast cancer cases and 2,902,468 females at risk in six Spanish provinces during the period 2010–2013. Breast cancer incidence risk increased with age and decreased with deprivation levels (i.e., women living in the most deprived areas had a lower breast cancer incidence risk). Females with breast cancer living in the most deprived areas (i.e., Q5) showed a rate of 98.5 cases per 100,000 vs. 127.1 cases per 100,000 among females living in the least deprived areas (i.e., Q1).

Table 2 shows the cancer incidence risk by sex, adjusted for deprivation, age, calendar year, and accounting for the correlation within census tracts for colorectal, lung, and breast

cancer during the period 2010–2013. After adjusting for age and calendar year (Model 3), the incidence risk of colorectal cancer among males living in the most deprived areas was 16% lower than for the males with colorectal cancer living in the least deprived areas (i.e., incidence rate ratio (IRR) Q5 vs. Q1: 0.84, 95% CI: 0.74–0.97). In females, there was no evidence of an association between deprivation and colorectal cancer incidence risk. There was weak evidence of an increased lung cancer incidence risk among the most deprived males (i.e., IRR Q5 vs. Q1: 1.18, 95% CI: 0.94–1.46) but not among women. For breast cancer, women from the least deprived areas showed an increased risk compared to women from the most deprived areas (i.e., IRR Q5 vs. Q1: 0.76, 95% CI: 0.68–0.85).

Table 2. Cancer incidence rates ratios by sex, adjusted for deprivation and age in Spain for the period 2010–2013.

| Colorectal Cancer | | | | | | |
|------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Variables | Females | | | Males | | |
| | Model 1 IRR (95% CI) | Model 2 IRR (95% CI) | Model 3 IRR (95% CI) | Model 1 IRR (95% CI) | Model 2 IRR (95% CI) | Model 3 IRR (95% CI) |
| Quintiles of SDI | | | | | | |
| Q1 | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Q2 | 1.02 (0.87–1.20) | 1.02 (0.87–1.20) | 0.99 (0.84–1.16) | 0.98 (0.86–1.12) | 0.94 (0.83–1.07) | 0.94 (0.83–1.07) |
| Q3 | 1.14 (0.98–1.34) | 1.15 (0.98–1.34) | 1.09 (0.93–1.27) | 0.99 (0.87–1.13) | 0.93 (0.82–1.05) | 0.93 (0.82–1.05) |
| Q4 | 1.13 (0.97–1.33) | 1.14 (0.97–1.34) | 1.04 (0.89–1.22) | 1.16 (1.01–1.32) | 1.02 (0.90–1.17) | 1.03 (0.91–1.18) |
| Q5 | 1.16 (0.98–1.38) | 1.17 (0.98–1.39) | 1.02 (0.86–1.22) | 0.99 (0.86–1.14) | 0.83 (0.72–0.95) | 0.84 (0.74–0.97) |
| Age in years | | | | | | |
| Per ten years increase | 1.02 (0.95–1.10) | 1.03 (0.96–1.11) | | 1.86 (1.81–1.92) | 1.86 (1.81–1.92) | |
| Period 2010–2013 | | | | | | |
| Per one year increase | | 1.58 (1.53–1.63) | | | 1.10 (1.04–1.16) | |
| Lung Cancer | | | | | | |
| Variables | Females | | | Males | | |
| | Model 1 IRR (95% CI) | Model 2 IRR (95% CI) | Model 3 IRR (95% CI) | Model 1 IRR (95% CI) | Model 2 IRR (95% CI) | Model 3 IRR (95% CI) |
| Quintiles of SDI | | | | | | |
| Q1 | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Q2 | 0.56 (0.32–0.97) | 0.56 (0.32–0.96) | 0.57 (0.33–0.98) | 1.06 (0.83–1.36) | 1.08 (0.85–1.38) | 1.08 (0.85–1.37) |
| Q3 | 1.02 (0.66–1.57) | 1.01 (0.66–1.56) | 1.03 (0.67–1.58) | 1.04 (0.83–1.30) | 1.07 (0.85–1.34) | 1.07 (0.85–1.34) |
| Q4 | 0.71 (0.45–1.13) | 0.72 (0.45–1.15) | 0.72 (0.45–1.14) | 1.14 (0.91–1.42) | 1.12 (0.90–1.39) | 1.12 (0.90–1.39) |
| Q5 | 0.80 (0.50–1.28) | 0.82 (0.51–1.31) | 0.76 (0.47–1.22) | 1.37 (1.09–1.71) | 1.17 (0.94–1.46) | 1.18 (0.94–1.46) |
| Age in years | | | | | | |
| Per ten years increase | 0.86 (0.62–1.18) | 0.85 (0.62–1.17) | | 2.03 (1.94–2.13) | 2.03 (1.94–2.13) | |
| Period 2011–2012 | | | | | | |
| Per one year increase | | 1.50 (1.40–1.61) | | | 1.00 (0.87–1.15) | |
| Breast Cancer—Females | | | | | | |
| Variables | Model 1 | | | Model 2 | | |
| | IRR (95% CI) |
| Quintiles of SDI | | | | | | |
| Q1 | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Q2 | 0.90 (0.80–1.00) | 0.91 (0.81–1.01) | 0.89 (0.80–0.99) | | | |
| Q3 | 0.83 (0.74–0.93) | 0.84 (0.75–0.94) | 0.81 (0.73–0.91) | | | |
| Q4 | 0.82 (0.74–0.92) | 0.83 (0.74–0.92) | 0.79 (0.71–0.89) | | | |
| Q5 | 0.79 (0.71–0.88) | 0.80 (0.72–0.89) | 0.76 (0.68–0.85) | | | |
| Age in years | | | | | | |
| Per ten years increase | 1.07 (1.03–1.12) | 1.06 (1.02–1.11) | | | | |
| Period 2010–2013 | | | | | | |
| Per one year increase | | 1.42 (1.40–1.44) | | | | |

IRR: Incidence rate ratio. Model 1: model adjusted for quintiles of the SDI. Model 2: model adjusted for quintiles of the SDI and age. Model 3: model adjusted for quintiles of the SDI, age, and year of diagnosis.

Figures 2–4 show the observed and age- and SES-standardized incidence smoothed rates by census tracts for colorectal, lung, and breast cancers. The pattern of smoothed rates for colorectal cancer was characterized by a higher cancer incidence risk in northern Spanish provinces (i.e., Bizkaia, Girona, and Navarra) than in southern provinces (i.e., Granada and Albacete) (Figure 2). For lung cancer, Granada showed a higher risk than Girona (Figure 3). However, for breast cancer, the same north–south pattern was present, showing higher smoothed incidence rates in the northern provinces (i.e., Gipuzkoa, Navarra, Girona, and Tarragona) compared to the southern province of Granada (Figure 4). Furthermore, there was a north–south pattern regarding the spatial heterogeneity of the smoothed rates. The pattern was characterized by a higher heterogeneity of the rates in northern provinces than southern provinces except for lung cancer, where Granada showed a homogenous higher risk than Girona. Overall, for breast and colorectal cancer, the risk was higher in the census

tracts from the province's capital (Supplementary Figures S4 and S6), while the opposite pattern was found for lung cancer (Supplementary Figure S5).

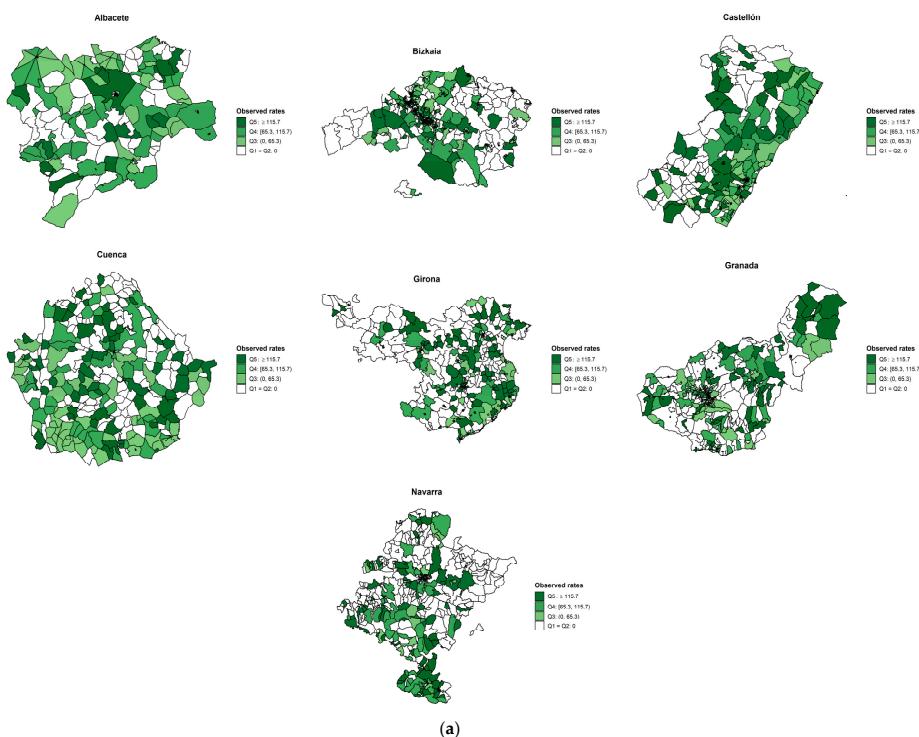
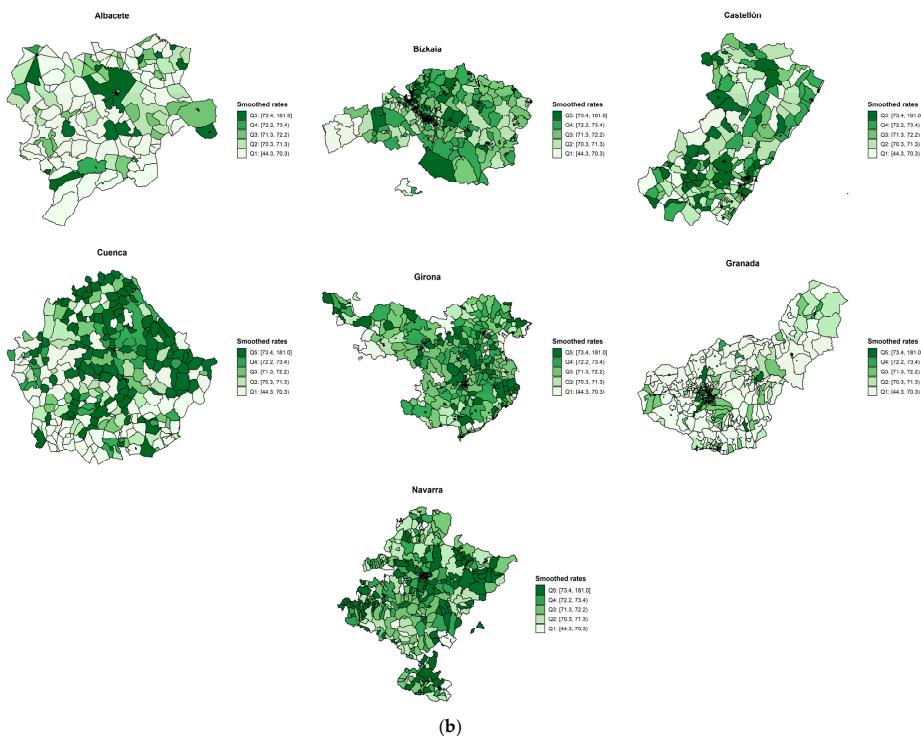


Figure 2. Cont.

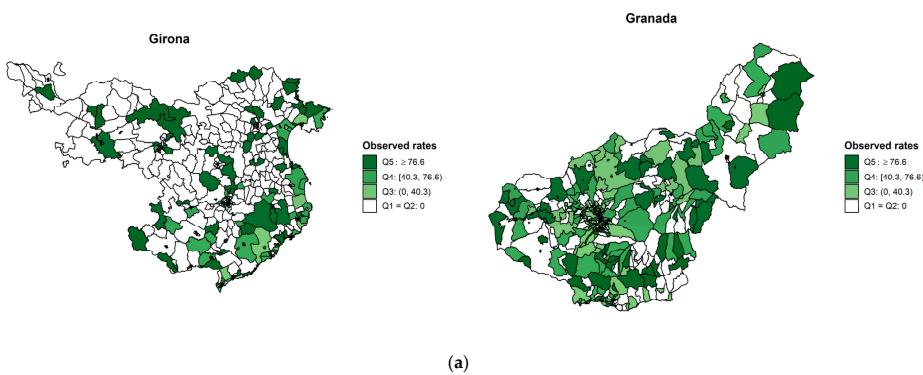
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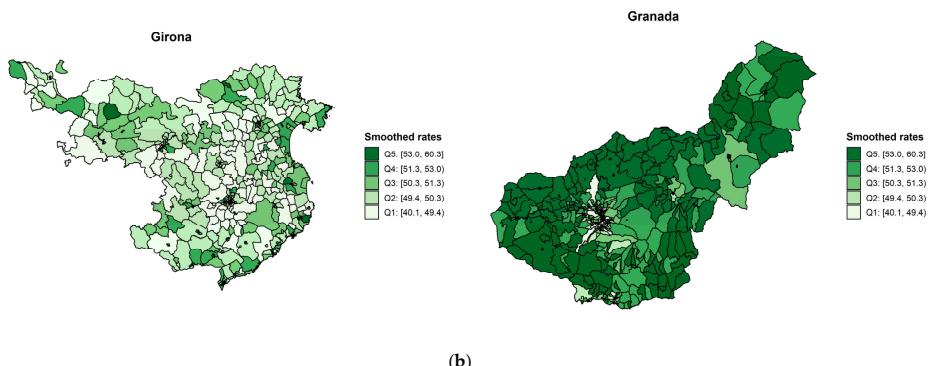
(b)

Figure 2. (a) Observed colorectal incidence rates and (b) smoothed cancer incidence rates adjusted for deprivation and age by census tract in seven Spanish provinces during the period 2010–2013.



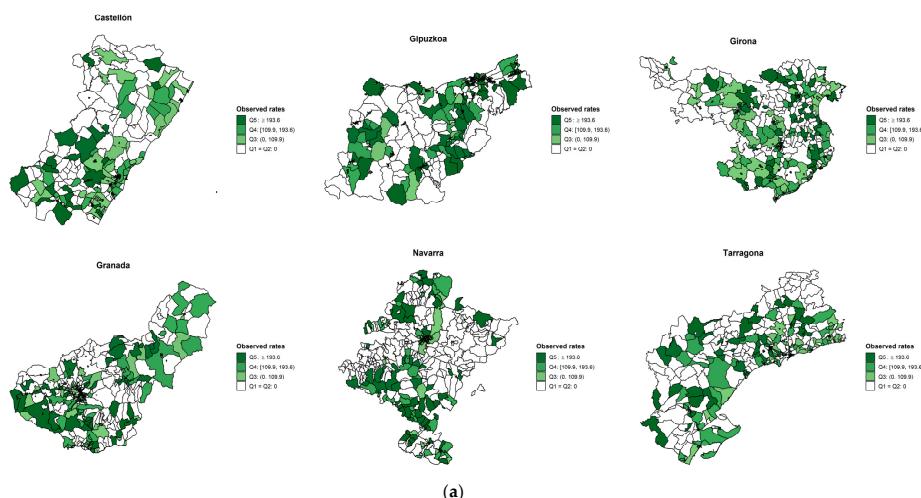
(a)

Figure 3. Cont.



(b)

Figure 3. (a) Lung observed incidence rates and (b) smoothed cancer incidence rates adjusted for deprivation and age by census tract in two Spanish provinces during the period 2011–2012.



(a)

Figure 4. Cont.

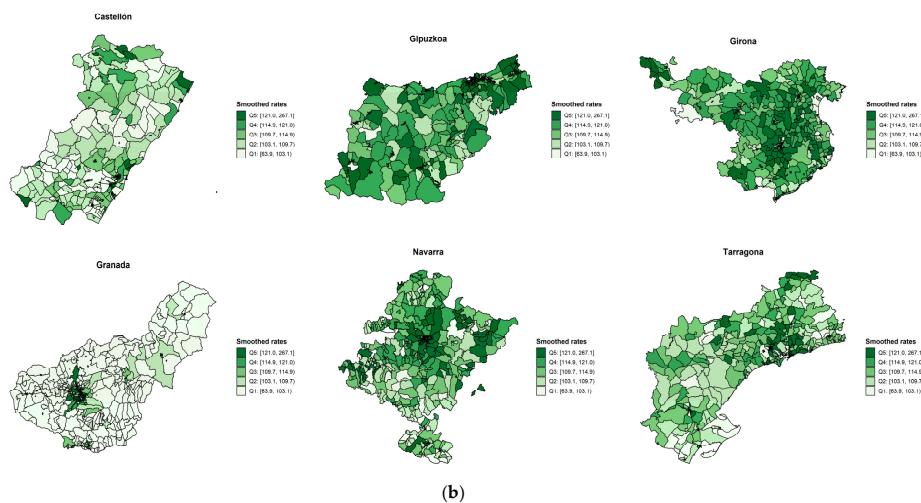


Figure 4. (a) Breast observed incidence rates and (b) smoothed cancer incidence rates adjusted for deprivation and age by census tract in seven Spanish provinces during the period 2010–2013.

Including the non-linear effect of age did not improve the overall model goodness of fit in the sensitivity analyses. Furthermore, the reported incidence rates were consistent with previously published evidence from official sources [17].

4. Discussion

We found that males with the lowest SES showed an increased risk of lung cancer incidence and a reduced risk of colorectal cancer incidence than those with the highest SES. Females with the lowest SES had a reduction in breast cancer incidence. Among women, we did not find evidence of an association between SES and lung or colorectal cancer.

Overall, our results are consistent with current evidence from population-based studies regarding cancer incidence and SES in Europe [18]. Low SES was associated with an increased risk of lung cancer in Denmark [19], England [20,21], France [22,23], Germany [24–26], Ireland [27], Italy [28], Slovenia [29], Sweden [30], and Scotland [31,32]. We found the same result in men, but the risk was not clear in women, perhaps due to the reduced number of cases. Furthermore, we found an inverse association between SES and breast cancer risk characterized by an increased risk among women with higher SES than those with lower SES. Likewise, the same pattern was found in England [21], France [22], Germany [24,25], Ireland [27], Italy [28], Scotland [32], and Slovenia [29]. However, there is a varying pattern of colorectal cancer incidence risk in Europe. Low SES was associated with an increased risk in England [21], Germany [25,26], and Scotland [31], while in other European countries, there was a reverse association or no association at all [18,23,24,27,29,33]. In our study, we found that males of more deprived areas were at a lower risk of colorectal cancer. We argue that it might be that there are two distinguished patterns of colorectal cancer risk in Europe related to lifestyle and cultural risk factors associated with SES [34]. However, more evidence is needed based on large periods and sample sizes. Furthermore, differences in the availability and impact of colorectal and breast cancer regional screening programs [35] might be associated with differences in the geographical distribution of cancer incidence rates.

4.1. Strengths

To the best of our knowledge, this is the first time that the association between area level SES and cancer incidence has been assessed in several Spanish provinces in a population-based study. Our study adds evidence regarding socioeconomic inequalities in cancer incidence around southern Europe. Furthermore, our results are consistent with other European countries and previous studies from Spain's northeast region [36].

The number of incident cancer cases reported by calendar year for the majority of cancer registries was exhaustive. Supplementary Tables S1–S3 show the distribution of the number of cases by anatomical site, year of diagnosis, and province. In the sensitivity analysis, we compared the reported incidence rates in our study by province and calendar year in the period 2011–2013 with official published statistics elsewhere [17]. Our study's reported cancer incidence rates were consistent with the European Cancer Information System [17]. Even if there was no information from all the Spanish provinces in our study, most of the Spanish population-based cancer registries participated in the study, and the socioeconomic north–south gradient was well represented.

4.2. Limitations

Individual information on SES is often difficult to obtain due to ethical issues. Usually, it is not available at the population level, and cancer registries use census tracts and aggregated deprivation measures. SDI is not used as a proxy of individual SES but a measure of the contextual effect of living in a census tract with a specific SES. We highlight the importance of interpreting findings at the population level to minimize ecological fallacy risk. It has recently been shown that, in England and Wales, the average socioeconomic status at the area level correlates poorly with the individual SES in higher heterogeneity areas (i.e., ecological fallacy) [37]. Moreover, in our study, the SDI was derived for 2011, while cancer incidence is measured for the period 2010–2013. However, evidence shows that the aggregated measures of socioeconomic inequalities are consistent over time [38].

Finally, we suggest caution in interpreting the spatial patterns we identified. There is no significant random variability due to the short period under study and the limited number of cancer cases.

5. Conclusions

The study evaluates the association between socioeconomic inequalities and colorectal, lung, and breast cancer incidence in nine Spanish provinces during the period 2010–2013. The findings are consistent with other European countries, showing the association between socioeconomic inequalities and lung cancer among men and reduced breast cancer incidence among women with lower SES. Studying the causes of these associations could help develop appropriate public health programs to promote health and reduce socioeconomic inequalities in cancer incidence in Spain. Further collaborative studies are required to update the assessment of socioeconomic inequalities in colorectal, lung, and breast cancers over time in Spain and to evaluate public health programs.

Supplementary Materials: The following are available online at <https://www.mdpi.com/article/10.3390/cancers13112820/s1>, Figure S1: Map of peninsular Spain with the provinces of the study highlighted by anatomical site: (a) colorectum, (b) lung, (c) breast, Figure S2: Spanish deprivation index (2011) and average income (in EUR) per person (2015) by census tract in Spain, with generalized additive model (GAM) smoothing, Figure S3: Quintiles of the Spanish Deprivation Index (SDI) by census tract in the capitals of the nine Spanish provinces under study, 2011, Figure S4: Colorectal cancer smoothed cancer incidence rates adjusted for deprivation and age by census tract in the area of the capital of province in seven Spanish provinces during the period 2010–2013, Figure S5: Lung cancer smoothed cancer incidence rates adjusted for deprivation and age by census tract in the area of the capital of province in two Spanish provinces during the period 2011–2012, Figure S6: Breast cancer smoothed cancer incidence rates adjusted for deprivation and age by census tract in the area of the capital of province in six Spanish provinces during the period 2010–2013, Table S1: Number of colorectal cancer cases, population at risk, and crude cancer incidence rates by year of diagnosis and

province in Spain during the period 2010–2013, Table S2: Number of lung cancer cases, population at risk, and crude cancer incidence rates by anatomical site, year of diagnosis, and province in Spain during the period 2011–2012, Table S3: Number of breast cancer cases, population at risk, and crude cancer incidence rates by anatomical site, year of diagnosis, and province in Spain during the period 2010–2013.

Author Contributions: D.R.-S., M.-J.S., and M.A.L.-F. designed the study. D.R.-S. and M.A.L.-F. analyzed the data and wrote the first manuscript draft. All the authors contributed to the data generation and curation, reviewed the study results, and drafted the manuscript's different versions. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The internal review board of the Andalusian School of Public Health (CP17/00206) and the biomedical ethics committee of the Department of Health of the Andalusian Regional Government (study 0072-N-18) approved the study protocol.

Informed Consent Statement: The study was carried out in accordance with the principles of the Declaration of Helsinki. No samples were used, all data accessed for the study were fully anonymized and informed consent was waived. The participant Cancer Registries comply with national and European data protection and privacy regulations.

Data Availability Statement: This research has been conducted using the Spanish National Statistics Institute data under application number BE181/2018 granting access to the corresponding population and mortality data. De-identified participant data from the Spanish cancer registries data are available via the High Resolution Studies on application. Proposals should be directed to the Spanish National Statistics Institute (<https://www.ine.es/>, accessed on 27 May 2021) and the High Resolution Studies (<http://www.hrstudies.eu/contacts.html>, accessed on 27 May 2021) to gain access; data requestors will need to sign a data access agreement.

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Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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Artículo 4 - Socio-economic inequalities in lung cancer mortality in Spain: a nation-wide study using area-based deprivation

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RESEARCH

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Socio-economic inequalities in lung cancer mortality in Spain: a nation-wide study using area-based deprivation

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Abstract

Background Lung cancer is the main cause of cancer mortality worldwide and in Spain. Several previous studies have documented socio-economic inequalities in lung cancer mortality but these have focused on specific provinces or cities. The goal of this study was to describe lung cancer mortality in Spain by sex as a function of socio-economic deprivation.

Methods We analysed all registered deaths from lung cancer during the period 2011–2017 in Spain. Mortality data was obtained from the National Institute of Statistics, and socio-economic level was measured with the small-area deprivation index developed by the Spanish Society of Epidemiology, with the census tract of residence at the time of death as the unit of analysis. We computed crude and age-standardized rates per 100,000 inhabitants by sex, deprivation quintile, and type of municipality (rural, semi-rural, urban) considering the 2013 European standard population (ASR-E). We further calculated ASR-E ratios between the most deprived (Q5) and the least deprived (Q1) areas and mapped census tract smoothed standardized lung cancer mortality ratios by sex.

Results We observed 148,425 lung cancer deaths (80.7% in men), with 73.5 deaths per 100,000 men and 17.1 deaths per 100,000 women. Deaths from lung cancer in men were five times more frequent than in women (ASR-E ratio = 5.3). Women residing in the least deprived areas had higher mortality from lung cancer (ASR-E = 22.2), compared to women residing in the most deprived areas (ASR-E = 13.2), with a clear gradient among the quintiles of deprivation. For men, this pattern was reversed, with the highest mortality occurring in areas of lower socio-economic level (ASR-E = 99.0 in Q5 vs. ASR-E = 86.6 in Q1). These socio-economic inequalities remained fairly stable over time and across urban and rural areas.

Conclusions Socio-economic status is strongly related to lung cancer mortality, showing opposite patterns in men and women, such that mortality is highest in women residing in the least deprived areas and men residing in the most deprived areas. Systematic surveillance of lung cancer mortality by socio-economic status may facilitate the assessment of public health interventions aimed at mitigating cancer inequalities in Spain.

Keywords Cancer, Lung cancer, Mortality, Health inequities, Socioeconomic disparities in health

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Introduction

Lung cancer was the main cause of cancer mortality during the year 2020, with an estimated burden of 1.2 million of deaths worldwide [1]. Between 80% and 90% of lung cancer cases are attributable to smoking, whereas the remaining cases are mainly related to carcinogens and environmental exposures, such as radon gas [2].

In Spain, lung cancer is the most deadly cancer in both sexes (1st in men, 3rd in women), with 22,930 deaths in 2020 [1]. The prevalence of smoking in Spain has traditionally been higher in men than in women, although a recent drastic reduction in the gap between the sexes has been observed [3]. During the last decades, and after several legislative measures [4], lung cancer mortality trends in Spain show opposite trends for each sex. While there has been an ascending trend in females, lung cancer mortality in males has been slowly decreasing after 1999, reflecting changes in smoking patterns [5, 6].

Reducing inequalities in cancer outcomes is a main priority of the European Union (EU) [7]. The EU recently created the European Cancer Inequalities Registry to help monitor and reduce cancer inequalities between and within EU Member States. Socio-economic status (SES) is known to play an important role in lung cancer outcomes: people with a lower SES are at higher risk of being diagnosed and dying from lung cancer, and have lower survival [8, 9].

In Europe, research has documented pervasive socio-economic inequalities in lung cancer mortality using either individual-level (e.g., education [10–15]) or area-based measures of SES [16–20]. Previous research suggests that similar socio-economic inequalities may be present in Spain. In particular, in a study of 2.6 million people at risk and 1,067 geocoded lung cancer cases, lower residential SES was associated with an increased risk of developing lung cancer among males but not females [21]. Moreover, when considering all-cause mortality in Spain, women and men residing in the most deprived areas lived 3.2 and 3.8 years less, respectively, than their counterparts residing in the least deprived areas [22].

To the best of our knowledge, in Spain, socio-economic inequalities in lung cancer mortality have only been investigated in specific provinces (e.g., Madrid [23]) or within large cities [16, 20, 24, 25]. For instance, the MEDEA project investigated lung cancer mortality as a function of an area-based deprivation index within 11 large cities [25]. This study reported different socio-economic inequalities for men and women, such that lung cancer mortality was higher for men but lower for women living in the more deprived areas. Similar results have been found in a recent nation-wide study considering socio-economic deprivation on the municipality level [26].

However, no study has examined lung cancer mortality in Spain nation-wide and using a comprehensive, small-area index of socio-economic deprivation. Such a study would provide valuable information on the existing inequalities in a geographically diverse area. The recently developed Spanish Deprivation Index (SDI) allows to characterize socio-economic deprivation in Spain and study its impact on diverse health outcomes [21, 27, 28]. This index uses area-based aggregated information from the national census data from 2011 and provides a standardized assessment of socio-economic deprivation by small areas [29]. In this context, the goal of this study was to describe lung cancer mortality in Spain as a function of socio-economic deprivation. Given the previously documented sex differences in lung cancer trends and outcomes, we aimed to do this separately for men and women.

Methods

All registered deaths from lung cancer during the period 2011–2017 in Spain were included. Lung cancer mortality data (ICD-10 codes C33-C34 [30]) in Spain during the period 2011–2017 by census tract, year, age and sex were obtained from the National Statistics Institute (protocol agreement BE099-2021). The census tract was defined as the census tract of residence at the time of death.

We used the layer of census tracts of the Spanish Census in 2011. Population data by census tract level, age group, and sex at 1st of January of 2011 were extracted from the National Statistics Institute [31]. Population data were completely merged with the layer of census tracts without losing any information.

To measure SES, we used an area-based deprivation index developed by the Spanish Society of Epidemiology, the Spanish Deprivation Index [29]. The Spanish Deprivation Index was created with data from the Spanish 2011 census conducted by the Spanish Statistical Office, and includes information from six indicators mainly related to employment and education: percentage of employed manual workers, percentage of unemployed manual workers, percentage of employed occasional workers, percentage of unemployed occasional workers, percentage of the population with insufficient education, and percentage of main homes without internet access [29]. The Spanish Deprivation Index was divided in quintiles (Q), where Q1 represents the least deprived areas (highest SES) and Q5 the most deprived areas (lowest SES). Each census tract was assigned with its corresponding SES quintile. The quintiles of the Spanish Deprivation Index by census tract were mapped.

The study protocol has received approval from the Internal Review Board of the Andalusian School of Public Health (CP17/00206), the Granada Provincial Research Review Committee, and the Biomedical Ethics

Committee of the Department of Health of the Andalusian Regional Government (study 0072-N-18). The research is in accordance with the principles embodied in the Declaration of Helsinki.

Expected lung cancer deaths for each census tract, sex, and age group were computed by multiplying the census tract population of each sex and age group by the overall age-sex-specific mortality crude rate. For each census tract, expected lung cancer deaths of each age group and sex were added to obtain expected lung cancer deaths by sex. For each sex, census tract smoothed standardized lung cancer mortality ratios (SMR) were computed using a conditional autoregressive model [32] based on fitting a spatial Poisson model with observed deaths as the dependent variable, expected deaths as an offset, and two random effect terms: census tract contiguity and census tract heterogeneity. For the smoothing of the lung cancer mortality ratios, we had to consider neighbouring census tracts. Only 3 census tracts had no neighbouring census tracts, and for these the closest census tract was chosen as an artificial neighbour. Models for each sex were fitted using INLA (Integrated Nested Laplace Approximations for Bayesian inference) with the R-INLA package and a simplified Laplace estimation of the parameters [33, 34].

Observed crude and age-standardized rates were computed for each quintile of deprivation, considering the 2013 European standard population (ASR-E) [35]. Mortality was analysed by SES quintile, sex, age group, and year. Deaths, crude rates and ASR-E were computed by

type of municipality (rural: <5,000 inhabitants; semi-rural: $\geq 5,000$ inhabitants and $<25,000$ inhabitants; and urban: $\geq 25,000$ inhabitants), sex and SES quintile. Observed age-specific rates were computed. Lung cancer mortality ASR-E ratios (Q5 vs. Q1) were computed by dividing the ASR-E for Q5 by the ASR-E for Q1. Standard error and 95% confidence interval were also computed for the ASR-E ratios adjusting a Poisson model [36].

We used R v.4.2.0 [37] for data management, statistical analysis and mapping. Packages ggplot2 v.3.4.0 [38] and sf v.1.0–9 [39] were used to produce all figures.

Results

During the period 2011–2017, 151,182 deaths from lung cancer were registered in Spain. Of all these deaths, 1.8% did not merge with the census tract layer and population of 2011, leaving 148,425 lung cancer deaths (80.7% in men) after the merging. Supplementary Fig. 1 shows the yearly distribution of lost deaths, which varies between 1.19% and 2012 and 2.43% in 2017.

The spatial distribution by census tract of the Spanish Deprivation Index quintiles is shown in Fig. 1. Overall, there was a north–south pattern, with lower deprivation in the north-east of Spain, Madrid city and its metropolitan area. Higher deprivation was found in southern Spain, the vast majority of the rural areas and the north-west.

Overall SMR by census tract for Spain, without considering SES, is shown in Fig. 2 for men (Fig. 2A) and women

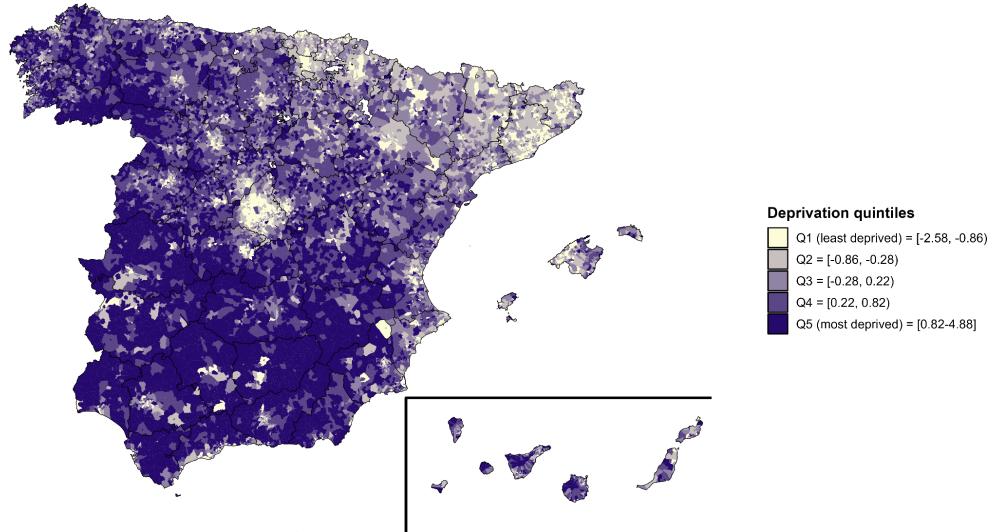
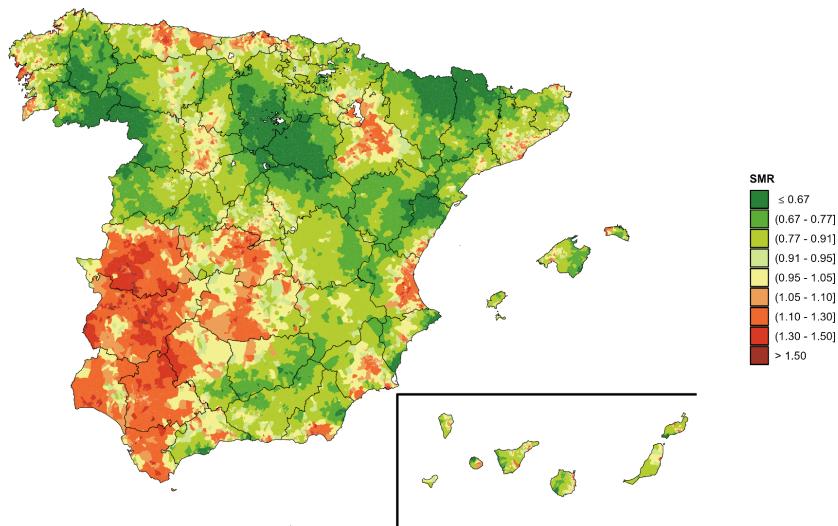
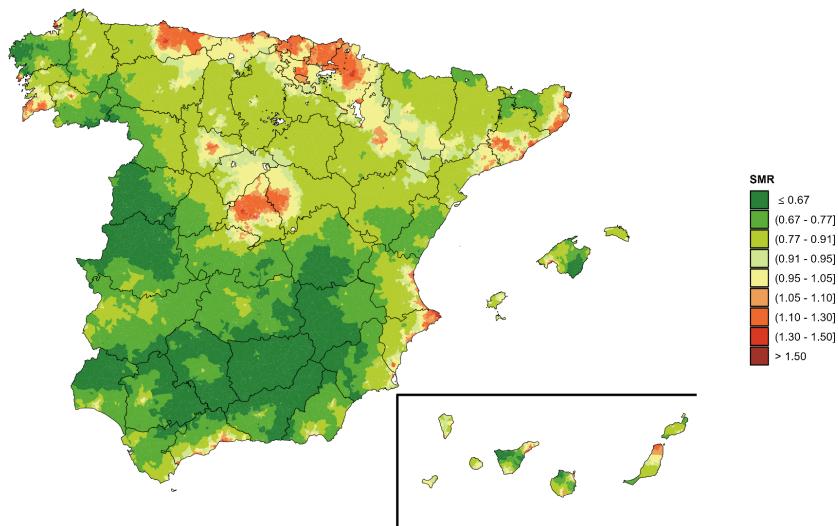


Fig. 1 Spanish Deprivation Index quintile by census tract

ALung cancer mortality.
Men, Spain, 2011-2017.**B**Lung cancer mortality.
Women, Spain, 2011-2017.**Fig. 2** Census tract smoothed standardized lung cancer mortality ratios (SMR) by sex (**A**: men; **B**: women). Spain, 2011–2017

(Fig. 2B). Lung cancer mortality in men was higher in the south-west regions of Spain, Zaragoza, and Valencia. The areas with lower lung cancer mortality in men are in the north of Spain (Huesca, Lleida, Soria, Burgos, Zamora, and Ourense). For women, lung cancer mortality is higher mainly in three areas, one located in Madrid and two in the north of Spain: one in Asturias and another one in Vizcaya, Álava, Guipúzcoa, and Navarra. The lower half of the Peninsula and the north-west have lower lung cancer mortality for women.

Table 1 shows the number of lung cancer deaths, population-year at risk, and lung cancer mortality crude rates and ASR-E per 100,000 inhabitants by sex and SES quintile. 148,425 lung cancer deaths were observed (80.7% in men), distributed in 73.5 deaths per 100,000 men and 17.1 deaths per 100,000 women. Deaths from lung cancer were five times more frequent in men than in women (ASR-E ratio: 5.3).

Women residing in the most affluent areas had higher mortality from lung cancer (Table 1), compared to women residing in the most deprived areas, with a clear gradient among the different quintiles of deprivation (ASR-E: 22.2 in Q1–18.3 in Q2–17.0 in Q3–15.1 in Q4–13.2 in Q5). The pattern was completely reversed for men (Table 1), where the highest lung cancer mortality occurred in men residing in the most deprived areas:

ASR-E for least deprived areas (Q1) and most deprived areas (Q5), respectively, were 86.6 and 99.0 per 100,000 men.

The consistency of the socio-economic inequalities found was supported by a sensitivity analysis using percentiles instead of quintiles to add more detail (Supplementary Fig. 2). When using percentiles, the mortality gradient was still clear in both sexes, with especially noticeable ASR-Es in the extremes of the SES distribution. For men, the highest standardized rate was obtained for men residing in P100 and P99 areas (lowest SES), with 121.9 and 110.7 deaths per 100,000 men respectively, while the lowest ASR-E was found in P1 and P2 areas (highest SES), with 78.9 and 80.2 deaths per 100,000 men respectively. In women, the lowest standardized rate was obtained for women residing in P92 areas, with 10.8 deaths per 100,000 women, whereas the highest ASR-E was found in P1 areas (highest SES), with 27.1 deaths per 100,000 women.

Considering the type of municipality, the lung cancer mortality ASR-E was higher in urban areas in both men and women of all quintiles of deprivation (Supplementary Tables 1, Supplementary Fig. 3). In men, we found a direct association between deprivation and lung cancer mortality in all types of municipalities, with higher mortality in urban and semi-rural areas. In women this

Table 1 Lung cancer mortality in Spain, 2011–2017, by sex and SES quintile. Number of deaths, population-year, crude mortality rate per 100,000 inhabitants, and ASR-E with 95% confidence interval (95% CI) per 100,000 inhabitants. (ASR-E: Age-standardized rates considering the 2013 European standard population)

| Sex | SES quintile | Deaths | Population-year | Crude mortality rate | ASR-E (95% CI) |
|-------|---------------------|----------------|--------------------|----------------------|-----------------------------|
| Men | Q1 (least deprived) | 22,069 | 36,841,952 | 59.9 | 86.6 (86.2–87.8) |
| | Q2 | 24,618 | 35,503,993 | 69.3 | 90.5 (90.1–91.7) |
| | Q3 | 25,391 | 33,345,074 | 76.1 | 93.5 (93.0–94.6) |
| | Q4 | 24,296 | 29,861,076 | 81.4 | 95.3 (94.8–96.5) |
| | Q5 (most deprived) | 23,409 | 27,430,214 | 85.3 | 99.0 (98.5–100.2) |
| | Total | 119,783 | 162,982,309 | 73.5 | 92.6 (92.4–93.1) |
| Women | Q1 (least deprived) | 7,918 | 39,652,172 | 20.0 | 22.2 (21.7–22.7) |
| | Q2 | 6,495 | 36,887,942 | 17.6 | 18.3 (17.9–18.7) |
| | Q3 | 5,798 | 34,002,808 | 17.1 | 17.0 (16.6–17.4) |
| | Q4 | 4,719 | 29,913,912 | 15.8 | 15.1 (14.7–15.6) |
| | Q5 (most deprived) | 3,712 | 26,894,308 | 13.8 | 13.2 (12.8–13.7) |
| | Total | 28,642 | 167,351,142 | 17.1 | 17.4 (17.2–17.6) |

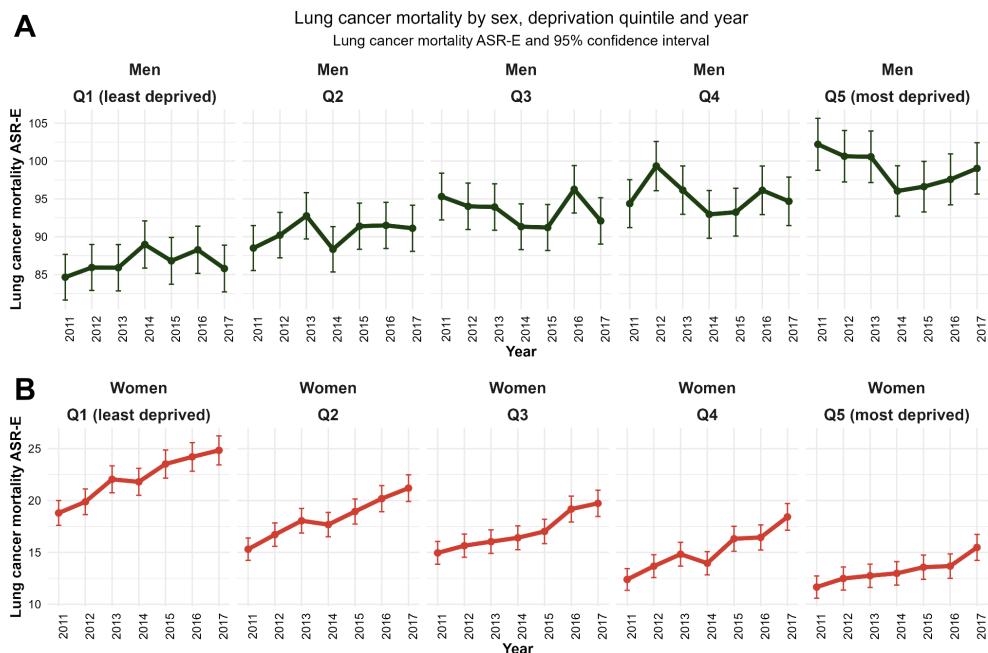


Fig. 3 Lung cancer mortality by sex, deprivation quintile, and year. Lung cancer mortality ASR-E per 100,000 inhabitants and 95% confidence interval. Spain, 2011–2017. (ASR-E: Age-standardized rates considering the 2013 European standard population)

Table 2 Lung cancer mortality ASR-E ratio (Q5 vs. Q1) and 95% confidence interval by sex and year. Spain, 2011–2017. (ASR-E: Age-standardized rates considering the 2013 European standard population)

| Sex | Year | ASR-E mortality ratio Q5 vs. Q1 (CI 95%) |
|-------|------|--|
| Men | 2011 | 1.21 (1.15–1.27) |
| | 2012 | 1.17 (1.12–1.23) |
| | 2013 | 1.17 (1.11–1.23) |
| | 2014 | 1.08 (1.03–1.13) |
| | 2015 | 1.11 (1.06–1.17) |
| | 2016 | 1.11 (1.05–1.16) |
| | 2017 | 1.15 (1.10–1.21) |
| Women | 2011 | 0.62 (0.56–0.69) |
| | 2012 | 0.63 (0.57–0.70) |
| | 2013 | 0.58 (0.52–0.64) |
| | 2014 | 0.60 (0.54–0.66) |
| | 2015 | 0.58 (0.52–0.64) |
| | 2016 | 0.56 (0.51–0.62) |
| | 2017 | 0.62 (0.57–0.69) |

association was reversed, and no clear distinction was found between rural and semi-rural areas.

In addition, the existing socio-economic inequalities in lung cancer mortality were consistent over time.

Figure 3 shows lung cancer mortality by sex, deprivation quintile, and year. An upward trend over time is observed for women residing in all areas (Fig. 3B), with the mortality rate being lower in most deprived areas. For women residing in the least deprived areas (Q1), the ASR-E per 100,000 women went from 18.8 to 2011 to 24.8 in 2017, whereas for women residing in the most deprived areas (Q5) the ASR-E per 100,000 women in 2011 was 11.7, compared to 15.5 in 2017. The time trend in men (Fig. 3A) is not clear, but there are relevant differences between deprivation quintiles.

In Table 2 and Supplementary Fig. 4 we show the lung cancer mortality ratio (ASR-E in Q5 divided by ASR-E in Q1) for each sex and year, demonstrating minor changes over time in men and women. For the whole period, men residing in the most deprived areas (Q5) had between 8% (in 2014) and 21% (in 2011) more lung cancer deaths than men residing in the most affluent areas (Q1). On the contrary, women residing in most affluent areas (Q1) had between 79% (2016) and 59% (2012) more lung cancer deaths than women residing in the most deprived areas (Q5). The evolution of the mortality ratio is relatively stable for both sexes for the whole period 2011–2017, suggesting that socio-economic differences by sex in lung

cancer mortality are not widening or narrowing over time.

The overall pattern of socio-economic inequalities by sex is also observed when analysing lung cancer mortality by SES quintile and age group using age-specific rates (Fig. 4). The mortality difference is detected from 50 years on for women (Fig. 4B), and between 35 and 69 years in men (Fig. 4A), with a gradient between the five quintiles of SES in both sexes.

Discussion

Overall, we found that lung cancer mortality varies strongly as a function of area-based deprivation, with opposite effects in men and women. Lung cancer mortality was highest among men residing in the most deprived areas and among women residing in the least deprived areas.

The documented socio-economic inequalities in men are in agreement with previous research in different European countries using diverse individual and

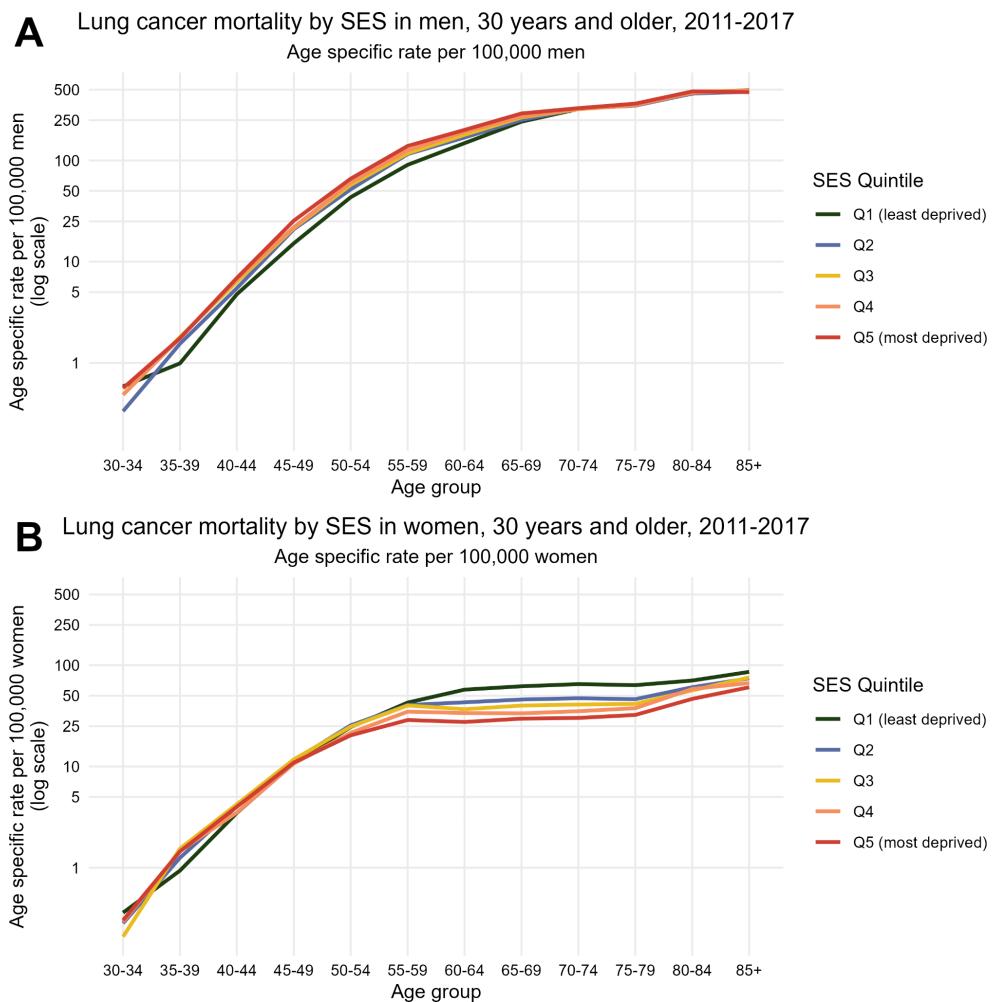


Fig. 4 Age-specific lung cancer mortality rate by sex (**A**: men, **B**: women) for persons ≥ 30 years old. Spain, 2011–2017. Age specific rate per 100,000 inhabitants

area-based indicators of SES [11–13, 15–18, 20, 23–26, 40–47]. In contrast, the association of SES with lung cancer mortality among women is less consistent and seems to be region-dependent. In particular, higher lung cancer mortality is consistently found for women of lower SES in Western and Northern European countries regardless of the SES measure used [13, 17, 18, 43]. The opposite effect – higher mortality among women with higher SES – has been found in Italy [11] and Spain [25, 26, 47]. In fact, several previous studies considering different European cities and regions have found this divergent pattern for these Mediterranean regions [10, 14, 16]. Given the time lag between smoking uptake and the occurrence of lung cancer (20–50 years depending on smoking intensity), these results are thought to reflect changes in smoking patterns [14, 26]. For instance, in Spain, smoking was more prevalent among men than women before the 1970s, after which smoking initiation started to be common among highly educated women, with less-educated women following suit in the 1980s [26]. As a result, Spain has experienced one of the largest increases in lung cancer mortality among women worldwide [48].

To look at more recent smoking trends, we used data from the Spanish National Health Survey [49], a large periodic representative survey of adults ≥ 15 years old residing in Spain. This survey is the main data source for the prevalence of smoking in Spain. The survey also records, since 1997, the individual educational level of respondents, one of the main components of the deprivation index used in this study. In Supplementary Fig. 5 we show the prevalence of smoking (in percentage) by sex, educational level, and year of the survey. In the last two decades, smoking prevalence has been declining over time in both men and women, and more strongly among the groups with higher education level. The decline in smoking prevalence is much less pronounced in men with low educational level, which may suggest that the higher lung cancer mortality in men residing in the most deprived areas may persist. The higher mortality in women residing in the least deprived areas could be partially due to the historically higher smoking prevalence in women with high educational level (university studies or secondary education). Because the prevalence in these groups has been declining steeply, we would expect socio-economic differences in lung cancer mortality for women to decrease in the following years. In fact, in a previous study on cancer incidence by SES in Spain, we found that lower SES was associated with an increased risk of lung cancer incidence among males, but no relationship was found for females [21].

Overall, with tobacco smoking being the main risk factor for lung cancer incidence, and the poor prognosis of the disease (5-year net survival in Spain: 13.2% [50]), differences in tobacco consumption patterns by SES seem

to be the underlying cause of the inequalities found in mortality. However, other factors such as financial issues, access to health services, or marginalization can affect lung cancer mortality [7].

The mapping of the SMR in our study shows a very similar pattern as other recent work for Spain and Portugal [51], with the present study considering a more recent period of mortality (2011–2017 instead of 2003–2012) and having a smaller unit of analysis (35,960 census tracts instead of 8,097 municipalities), characteristics that can produce stronger relationships between SES and cancer outcomes [52, 53].

The socio-economic inequalities in lung cancer mortality remained fairly stable over time and across urban and rural areas. The higher lung cancer mortality we found in urban areas is in accordance with a previous research conducted in the Madrid Autonomous Region [23], where after adjusting for deprivation quintile and air pollution, rural areas had a rate ratio of lung cancer mortality of 0.73 in men aged < 65 years, 0.84 in men aged ≥ 65 years, 0.51 in women aged < 65 years and 0.66 in women aged ≥ 65 years, considering the city of Madrid (urban area) as reference.

The overall lung cancer mortality rates of our study were aligned with the information provided for Spain in the Global Cancer Observatory (GCO) [1] and the European Cancer Information System (ECIS) [54]. Following the lung cancer mortality trends in Spain, which are increasing in females and decreasing in males [6], the ASR-E obtained in our study (2011–2017) were 92.6 and 17.4 deaths per 100,000 inhabitants in males and females respectively, which are consistent with the estimation of ECIS for 2020: 80.8 deaths per 100,000 males and 21.3 deaths per 100,000 females [54]. For comparison with the GCO data, we computed the age-standardized rates considering the World standard population (ASR-W) [55]. For Spain during the period 2011–2017, ASR-W were 38.8 and 8.6 deaths per 100,000 inhabitants for males and females respectively, in accordance with the estimation of GCO of 33.2 deaths per 100,000 males and 10.4 per 100,000 females [1].

One limitation of this study is that the deprivation index and population data are referred to 2011, whereas the mortality data covers a longer period (2011–2017). Deprivation may have changed during 2011–2017, nevertheless we argue that aggregated measures of socio-economic inequalities are likely to be fairly consistent over time. Moreover, the use of the European Index of Deprivation [56] could have facilitated the replication and comparison of the present study in the European context, but unfortunately this index is not updated for 2011 in Spain.

Whereas the deprivation index is not based on direct information about income, in a previous study we

discovered that, at the census tract level, this deprivation index and the average income per person are correlated in Spain [21]. An additional constraint of the research is that a small percentage of lung cancer deaths (less than 2% overall) were lost due to changes in the cartography over time. The loss is higher for the last years of the period 2011–2017 (Supplementary Fig. 1), especially after 2013, but there are no reasons to believe this is uneven across the levels of SES. Unfortunately, geocoded deaths or a list of changes over time of the different census tract layers are not available.

One of the main strengths of the study is the use of exhaustive mortality data collected by an official institution. Although some issues with the coding of the cause of death are plausible [57, 58], for lung cancer this is not as likely as in other anatomical locations such as uterus [59, 60]. Finally, the use of nation-wide mortality data covering several years allowed us to describe socio-economic inequalities in a large geographically diverse area.

More broadly, the current results show the need for interventions targeting the social determinants of health, accompanied by regular monitoring over time using standardized measures to better understand the effects of policies on lung cancer mortality. Forthcoming interventions need to consider SES as one of the main components to maximize the effect produced. For instance, Europe's Beating Cancer Plan promotes the implementation of lung cancer screening with low-dose computed tomography in the European Union [61]. In Spain, multiple scientific societies are piloting the CASSANDRA project (Cancer Screening, Smoking Cessation and Respiratory Assessment), aiming to assess the feasibility of population screening through recruitment of patients in more than 20 public, private, and primary care centres. Previous works suggest that novel interventions such as lung cancer screening can widen the existing mortality inequalities [62–65]. A recent systematic review [62] found that, in the United States, lower household income was linked with lower screening eligibility [63], and lower income patients were less likely to complete screening or have the intention to be screened [64, 65]. A key premise behind the success of lung cancer screening is the identification of high-risk profiles (e.g. heavy smokers or ex-smokers who used to smoke heavily). The current results suggest that SES should be evaluated as another relevant variable to include in profiling.

A complex approach involving both individual-level and population-level interventions is needed to reduce the extent of the socio-economic inequalities we found in our study. Improving access to healthcare in lower socio-economic groups (specially in men) and reducing the exposure to risk factors like smoking or environmental pollutants could reduce the inequalities in lung cancer

mortality, while more knowledge about the root causes is required for such interventions to be more effective.

Conclusions

Socio-economic status is strongly related to lung cancer mortality, showing opposite patterns in men and women, such that mortality is highest in women residing in the least deprived areas and men residing in the most deprived areas. Documenting socio-economic inequalities in lung cancer mortality could help direct policies and interventions aiming to reduce inequalities. Systematic surveillance of lung cancer mortality by socio-economic status may facilitate the assessment of public health interventions aimed at mitigating cancer health inequalities in Spain.

List of abbreviations

| | |
|-------|--|
| ASR-E | Age-standardized rates considering the 2013 European standard population |
| ASR-W | Age-standardized rates considering the World standard population |
| ECIS | European Cancer Information System |
| GCO | Global Cancer Observatory |
| SES | Socio-economic status |
| SMR | Census tract smoothed standardized lung cancer mortality ratios |

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12939-023-01970-y>.

Supplementary Material 1

Supplementary Material 2

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Authors' contributions

DRS and MRB obtained the data. DRS, PFN and ON designed the study. DRS and PFN analysed the data. DRS wrote the first draft of the manuscript. All authors contributed to data curation, reviewed the results of the study, and drafted the different versions of the manuscript.

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Data Availability

Population datasets and cartography are available publicly at the Spanish National Statistics Institute webpage (<https://www.ine.es/en/index.htm>). Mortality datasets analysed during the current study are not accessible to the public as they are subject to confidentiality restrictions. However, they can be obtained from the Spanish National Institute of Statistics on reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol has received approval from the Internal Review Board of the Andalusian School of Public Health (CP17/00206), the Granada Provincial Research Review Committee, and the Biomedical Ethics Committee of the Department of Health of the Andalusian Regional Government (study 0072-N-18). The research is in accordance with the principles embodied in the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Disclaimer

This article presents an independent research. The views expressed are those of the authors, and not necessarily those of the Carlos III Institute of Health.

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Anexo 1

Influencia del nivel socioeconómico en la supervivencia de cáncer de mama en mujeres

En este anexo se muestra, de manera resumida, el estudio de la influencia del nivel socioeconómico en la supervivencia de cáncer de mama en mujeres, utilizando por primera vez las tablas de vida generadas en el artículo 2 asociado a esta tesis doctoral.

Introducción

El cáncer de mama es el cáncer más frecuente en mujeres en España y tiene una alta supervivencia neta (86 % a los 5 años en 2008-2013). Además, gracias a importantes avances de diagnóstico temprano y terapéuticos, la supervivencia del cáncer de mama ha mejorado considerablemente en las últimas décadas.

En España no existen estudios previos que investiguen la influencia del nivel socioeconómico en la supervivencia de cáncer de mama. A nivel europeo, se ha encontrado que pacientes que viven en áreas de bajo nivel socioeconómico tienen peor supervivencia en varios países: Italia, Países Bajos, Irlanda, Francia, Alemania y Reino Unido.

Métodos

Se incluyeron los casos nuevos de cáncer de mama (C50 según la Clasificación Internacional de Enfermedades Oncológicas, 3^a edición) diagnosticados entre 2010 y 2014 en 6 provincias españolas que representaban el 9,3 % de la población española: Castellón, Gipuzkoa, Girona, Granada, Navarra y Tarragona. Como es habitual en los análisis de supervivencia, se excluyeron aquellos casos diagnosticados solo por certificado de defunción o solo por autopsia.

Las direcciones postales de residencia de cada mujer en el momento del diagnóstico fueron geocodificadas usando la aplicación GEO_CIBER. A cada caso se le asignó el índice de privación de Duque et al. dividido en quintiles.

Se realizó un seguimiento de los casos para determinar su estado vital con un mínimo de seguimiento de 5 años. La supervivencia observada (SO) se derivó usando el estimador de Kaplan-Meier. La supervivencia relativa, que estima la supervivencia neta, se modelizó mediante modelos paramétricos flexibles ajustados por quintil de privación, provincia, edad y estadio al diagnóstico. Para ello, se usaron las tablas de vida por provincia, edad, año y nivel socioeconómico generadas en el artículo 2. Finalmente, se calculó la razón de exceso de riesgo (RER) por nivel socioeconómico.

Resultados

Se analizaron 3.253 casos de cáncer de mama en mujeres. En la tabla 5 se muestra la distribución de casos y su supervivencia observada a 5 años.

Tabla 5. Distribución de casos de cáncer de mama en mujeres y supervivencia observada a 5 años.

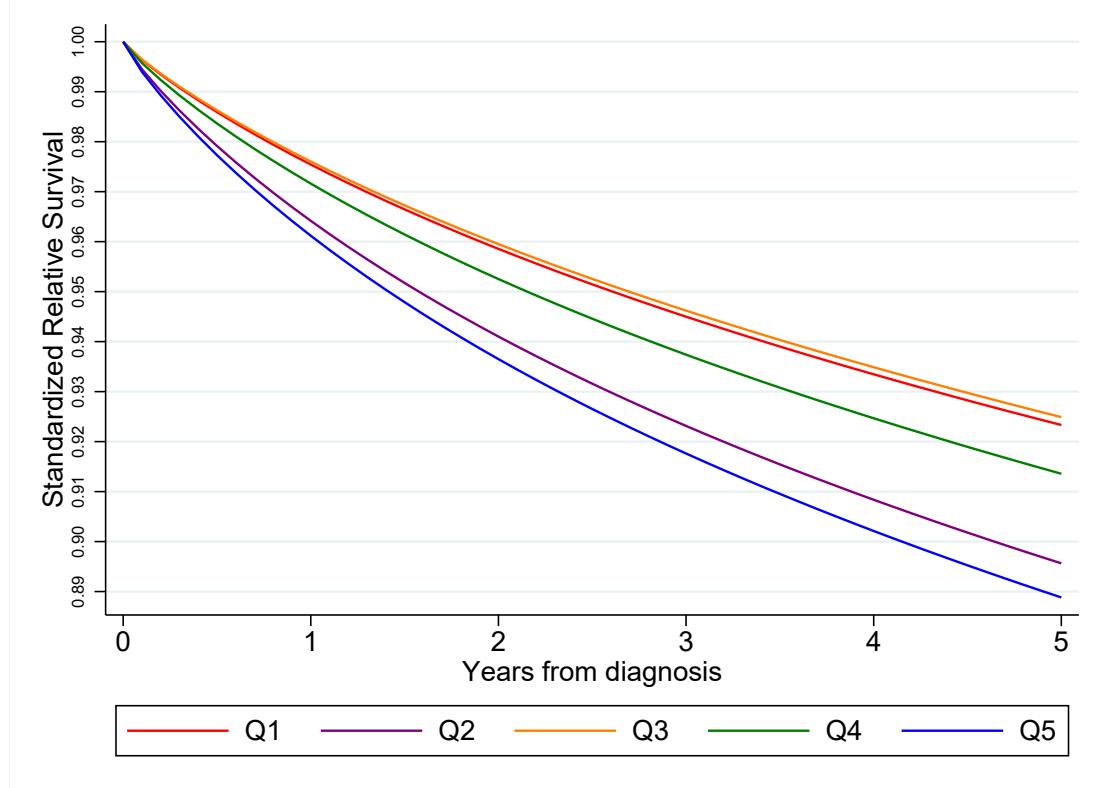
| | | Casos (%) | SO a 5 años |
|-----------------------------|----------------------|------------------------|---------------|
| | Total | 3.253 (100,0 %) | 83,4 % |
| Quintil de privación | Q1 (menor privación) | 673 (20,7 %) | 85,7 % |
| | Q2 | 933 (28,7 %) | 82,6 % |
| | Q3 | 820 (25,2 %) | 85,0 % |
| | Q4 | 514 (15,8 %) | 82,2 % |
| | Q5 (mayor privación) | 313 (9,6 %) | 78,2 % |
| Grupo de edad | 15-49 | 913 (28,1 %) | 93,0 % |
| | 50-69 | 1.438 (44,2 %) | 90,7 % |
| | 70-79 | 498 (15,3 %) | 76,9 % |
| | 80+ | 404 (12,4 %) | 43,7 % |
| Provincia | Castellón | 559 (17,2 %) | 83,2 % |
| | Gipuzkoa | 465 (14,3 %) | 85,8 % |
| | Girona | 776 (23,9 %) | 81,2 % |
| | Granada | 460 (14,1 %) | 82,1 % |
| | Navarra | 451 (13,8 %) | 88,5 % |
| | Tarragona | 542 (16,7 %) | 81,5 % |
| Año de diagnóstico | 2010 | 547 (16,8 %) | 80,8 % |
| | 2011 | 1.943 (59,7 %) | 82,8 % |
| | 2012 | 312 (9,6 %) | 84,0 % |
| | 2013 | 383 (11,8 %) | 88,3 % |
| | 2014 | 68 (2,1 %) | 89,7 % |
| Estadio | I | 1.265 (38,9 %) | 95,9 % |
| | II | 1.098 (33,8 %) | 88,8 % |
| | III | 518 (15,9 %) | 74,1 % |
| | IV | 192 (5,9 %) | 27,6 % |
| | Desconocido | 180 (5,5 %) | 48,9 % |
| Tipo de detección | Cribado | 1.225 (38,5 %) | 94,0 % |
| | Sintomático | 1.956 (61,5 %) | 77,2 % |

SO: Supervivencia observada.

El grupo de edad más frecuente fue de 50 a 69 años, grupo donde se realiza el cribado de cáncer de mama. La mayoría de los casos fueron diagnosticados en el año 2011 y tuvieron un diagnóstico temprano, con un 72,6% de los casos diagnosticados en estadios I y II. La supervivencia observada global fue del 83,2% a los 5 años. En general, se observó que la supervivencia observada disminuyó con el aumento de la edad y el estadio. La supervivencia observada ha mejorado a lo largo del tiempo y es muy alta en casos detectados por cribado (94,0% frente al 77,2% en los casos sintomáticos). Por nivel socioeconómico no se encontró un patrón claro, aunque la supervivencia observada fue 7,5% mayor en las áreas con menor privación (SO=85,7%) que en las áreas con mayor privación (SO=78,2%).

La supervivencia relativa a los 5 años, sin considerar el nivel socioeconómico, fue del 91,0%. En la Figura 26 se muestra la supervivencia relativa marginal por nivel socioeconómico. Si bien no existe un gradiente claro entre quintiles de privación, se observa que la brecha entre el nivel socioeconómico más alto (Q1) y el nivel socioeconómico más bajo (Q5) se amplía con el tiempo: es de 1,3% a 1 año, de 2,5% a 3 años y de 3,2% a 5 años.

Figura 26. Curva de supervivencia relativa marginal de cáncer de mama en mujeres por nivel socioeconómico.



En el modelo ajustado por edad, tipo de diagnóstico, estadio y año se encontraron diferencias significativas entre la RER del nivel socioeconómico más alto (Q1) y la del nivel socioeconómico más bajo (Q5) (Tabla 6). Todas las variables salvo el año de diagnóstico fueron relevantes en este modelo final.

Tabla 6. Razones de exceso de riesgo derivada de los modelos paramétricos flexibles ajustados secuencialmente. Todos los modelos están ajustados por edad.

| | | Modelo 1 | Modelo 2 | Modelo 3 | Modelo 4 |
|-----------------------------|-----------------------|--------------|--------------|--------------|--------------|
| Quintil de privación | Q1 | (Ref) | (Ref) | (Ref) | (Ref) |
| | Q2 | 1,22 | 1,34 | 1,52* | 1,48 |
| | Q3 | 0,61* | 0,69 | 1,00 | 0,97 |
| | Q4 | 1,25 | 1,38 | 1,38 | 1,33 |
| | Q5 | 1,77* | 1,81* | 1,66* | 1,61* |
| Tipo de diagnóstico | Cribado | | (Ref) | (Ref) | (Ref) |
| | Sintomático | | 5,30* | 1,90* | 1,86* |
| Estadio | VI | | | (Ref) | (Ref) |
| | III | | | 0,15* | 0,15* |
| | II | | | 0,03* | 0,04* |
| | I | | | 0,01* | 0,01* |
| | Desconocido | | | 0,22* | 0,22* |
| Año de diagnóstico | (Incremento de 1 año) | | | | 0,90 |

* p-valor <0,05; RER: Razones de exceso de riesgo.

Discusión y conclusiones

La supervivencia del cáncer de mama en mujeres está altamente influenciada por el tipo de diagnóstico, el estadio y la edad. Se observan desigualdades en el pronóstico según nivel socioeconómico, incluso tras ajustar por edad, año, estadio y tipo de diagnóstico.

La supervivencia del cáncer de mama encontrada en este estudio es alta comparada con la reportada por REDECAN (a 5 años, 91,0 % vs 85,5 %), si bien se comparan períodos y provincias diferentes. Son necesarias medidas para reducir las desigualdades socioeconómicas en la supervivencia del cáncer de mama.

Anexo 2

Influencia del nivel socioeconómico en la mortalidad por cáncer de colon-recto y mama

El análisis realizado para dar respuesta al objetivo específico 4 se ha repetido para la mortalidad por colon-recto (C18-C21 en CIE-10) y mama (C50) para conocer de forma completa el efecto del nivel socioeconómico en la incidencia y mortalidad de los cánceres de pulmón, colon-recto y mama. En este anexo se muestran los resultados de esos análisis.

Mortalidad por cáncer de colon-recto

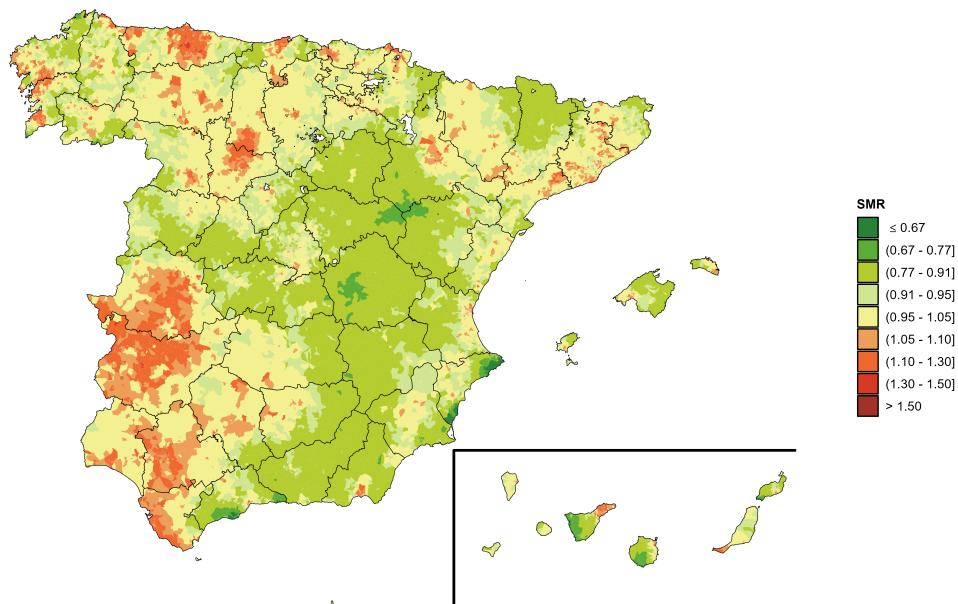
En España durante 2011-2017 hubo 106.723 defunciones por cáncer de colon-recto, siendo la mayoría en hombres (59,4 %, 63.355 muertes).

Observando la distribución espacial de la mortalidad por cáncer de colon-recto (Figura 27), el patrón fue muy similar en hombres y mujeres. En general, las zonas de mayor mortalidad estaban en el oeste de la península, destacando especialmente Extremadura y el suroeste andaluz.

Figura 27. Razón suavizada estandarizada de mortalidad por cáncer de colon-recto por sexo (A: hombres, B: mujeres). España, 2011-2017.

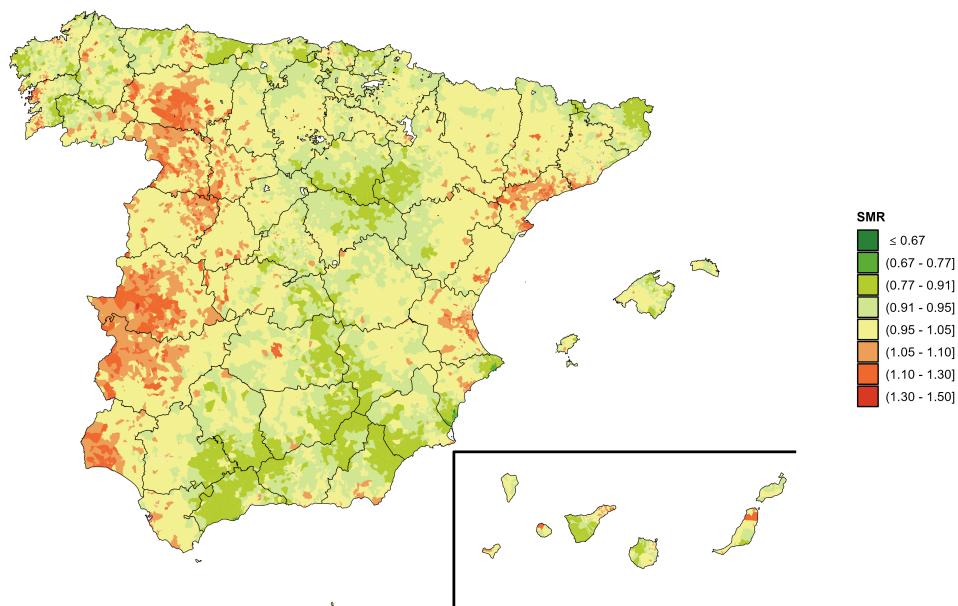
A

Mortalidad por cáncer de colon-recto.
Hombres, España, 2011-2017.



B

Mortalidad por cáncer de colon-recto.
Mujeres, España, 2011-2017.



Si bien en los resultados del objetivo específico 3 se encontró una mayor incidencia de cáncer de colon-recto entre hombres de nivel socioeconómico más alto, este resultado no se mantuvo en la mortalidad (Tabla 7). De hecho, en hombres la ASR-E fue muy similar entre los niveles socioeconómicos más altos y más bajos (49,9 y 49,7 respectivamente). En mujeres se observa un cierto gradiente en la mortalidad por quintiles (ASR-E: 24,4 en Q1 - 24,3 - 23,6 - 23,8 - 23,5 en Q5), aunque las diferencias son pequeñas y los intervalos de confianza al 95 % se superponen (Tabla 7).

Tabla 7. Mortalidad por cáncer de pulmón por sexo y quintil de privación, España, 2011-2017. Número de defunciones, tasa bruta por 100.000 habitantes y tasa estandarizada por la población estandarizada europea de 2013 por 100.000 habitantes con intervalo de confianza al 95 %.

| Sexo | Quintil de privación | N | TB | ASR-E 2013 (IC 95 %) |
|----------------|----------------------|--------|------|-------------------------|
| Hombres | Q1 (menor privación) | 12.090 | 32,8 | 49,9 (49,4 - 50,5) |
| | Q2 | 13.329 | 37,5 | 51,7 (51,2 - 52,3) |
| | Q3 | 13.722 | 41,2 | 52,7 (52,1 - 53,2) |
| | Q4 | 12.623 | 42,3 | 50,7 (50,1 - 51,2) |
| | Q5 (mayor privación) | 11.591 | 42,3 | 49,7 (49,2 - 50,2) |
| Mujeres | Q1 (menor privación) | 9.386 | 23,7 | 24,4 (23,9 - 25,0) |
| | Q2 | 9.332 | 25,3 | 24,3 (23,7 - 24,8) |
| | Q3 | 8.831 | 26,0 | 23,6 (23,0 - 24,1) |
| | Q4 | 8.287 | 27,7 | 23,8 (23,2 - 24,3) |
| | Q5 (mayor privación) | 7.532 | 28,0 | 23,5 (23,0 - 24,1) |

N: Número de defunciones; TB: Tasa bruta por 100.000 habitantes; ASR-E: Tasa estandarizada por la población europea de 2013 por 100.000 habitantes; IC 95 %: Intervalo de confianza al 95 %.

El análisis de la mortalidad por cáncer de colon-recto por años (Figura 28) o grupos de edad (Figura 29) no permite extraer ninguna conclusión relevante.

Figura 28. Mortalidad por cáncer de colon-recto por sexo, quintil de privación y año. ASR-E por 100.000 habitantes e intervalo de confianza al 95 %. España, 2011-2017.

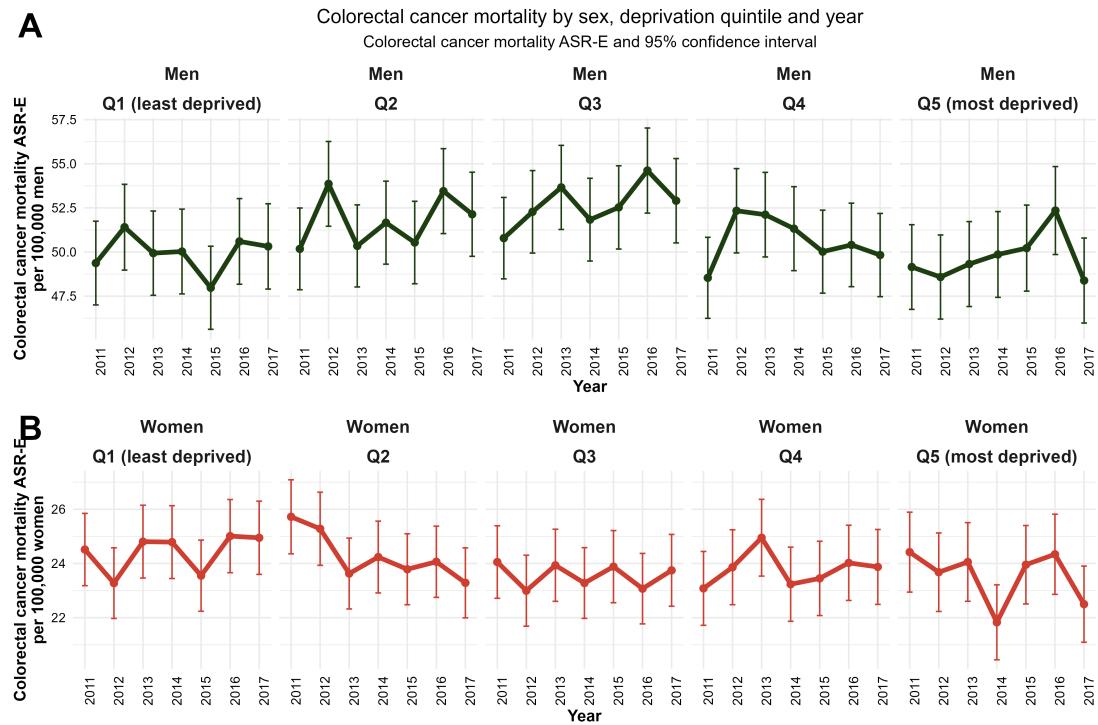
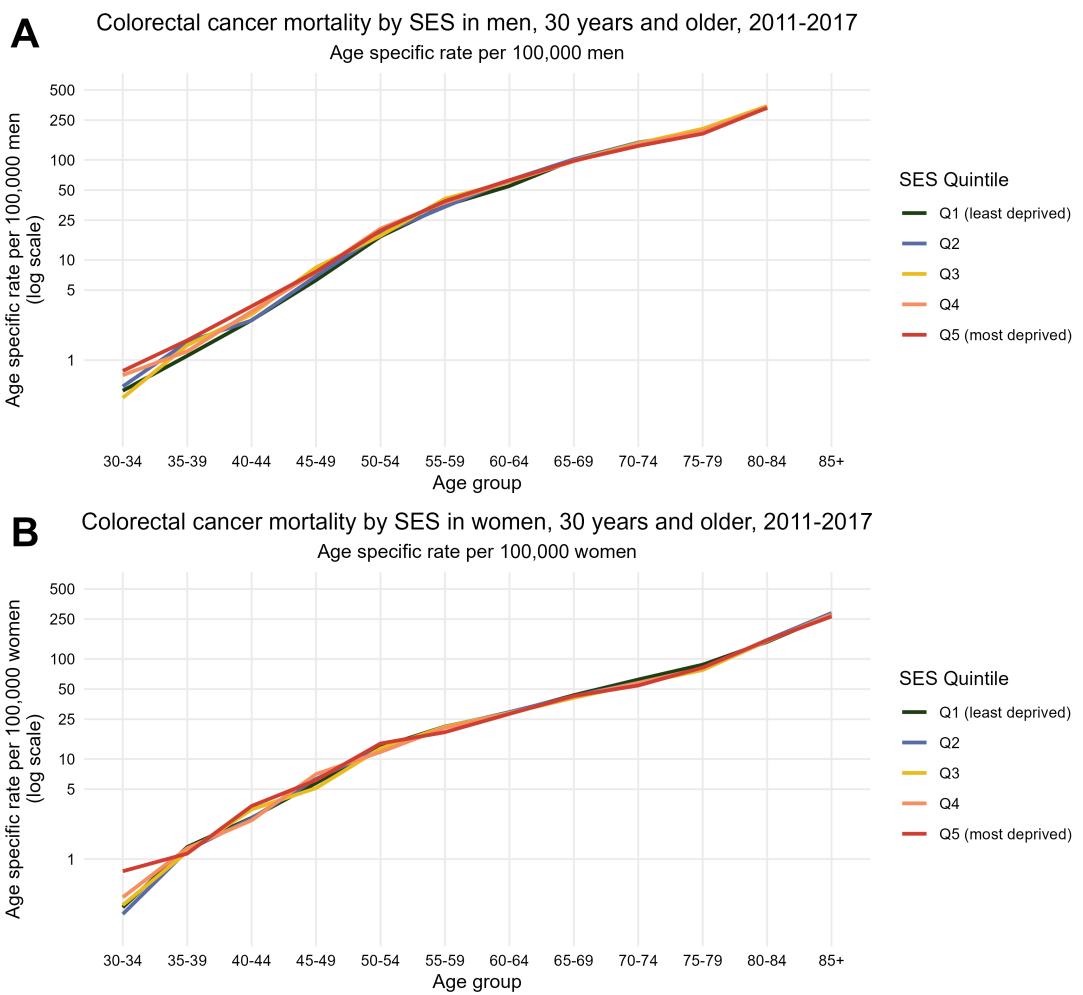


Figura 29. Mortalidad por cáncer de colon-recto por sexo (A: hombres, B: mujeres), grupo de edad y quintil de privación para adultos ≥ 30 años. Tasa específica por edad por 100.000 habitantes, escala logarítmica. España, 2011-2017.

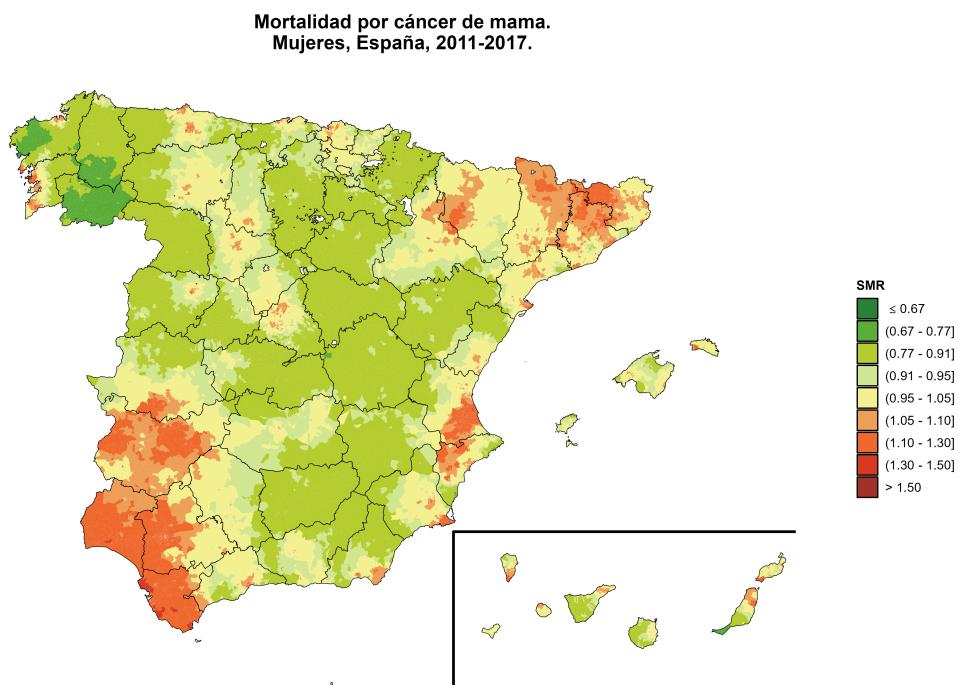


Mortalidad por cáncer de mama en mujeres

Como se mencionaba en la introducción, el cáncer de mama es un tipo de cáncer poco incidente en hombres. Como consecuencia, durante el periodo 2011-2017, en España se produjeron 623 defunciones por cáncer de mama en hombres, frente a las 43.479 defunciones en mujeres. Por este motivo, no se van a analizar las defunciones por cáncer de mama en hombres.

En la Figura 30 se observan que las zonas con mayor mortalidad en mujeres por cáncer de mama fueron Badajoz, Huelva, Cádiz, el oeste de Sevilla, Valencia y el norte de Cataluña. En contraposición, la mortalidad fue más baja en Galicia, especialmente en la provincia de Ourense.

Figura 30. Razón suavizada estandarizada de mortalidad por cáncer de mama en mujeres. España, 2011-2017.



Las mujeres de nivel socioeconómico más alto tuvieron una mayor probabilidad de fallecer por cáncer de mama (Tabla 8), existiendo además un gradiente entre quintiles.

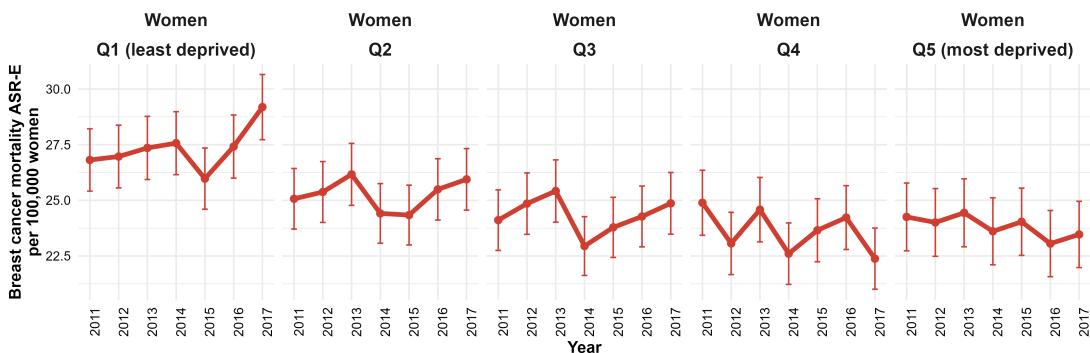
Tabla 8. Mortalidad por cáncer de mama en mujeres por quintil de privación, España, 2011-2017. Número de defunciones, tasa bruta por 100.000 mujeres y tasa estandarizada por la población estandarizada europea de 2013 por 100.000 mujeres con intervalo de confianza al 95 %.

| Sexo | Quintil de privación | N | TB | ASR-E 2013 (IC 95 %) |
|----------------|----------------------|--------|------|-------------------------|
| Mujeres | Q1 (menor privación) | 10.436 | 26,3 | 27,3 (26,8-27,9) |
| | Q2 | 9.449 | 25,6 | 25,3 (24,7-25,8) |
| | Q3 | 8.766 | 25,8 | 24,3 (23,8-24,9) |
| | Q4 | 7.778 | 26,0 | 23,6 (23,1-24,2) |
| | Q5 (mayor privación) | 7.050 | 26,2 | 23,8 (23,3-24,4) |

N: Número de defunciones; TB: Tasa bruta por 100.000 mujeres; ASR-E: Tasa estandarizada por la población europea de 2013 por 100.000 mujeres; IC 95 %: Intervalo de confianza al 95 %.

En la evolución temporal de la mortalidad por cáncer de mama en mujeres (Figura 31), llama la atención el aumento de la mortalidad en el nivel socioeconómico más alto (Q1, primer panel de la Figura 31), frente al descenso de la mortalidad en los niveles socioeconómicos más bajos (Q4 y Q5).

Figura 31. Mortalidad por cáncer de mama en mujeres por quintil de privación y año. ASR-E por 100.000 habitantes e intervalo de confianza al 95 %. España, 2011-2017.



Teniendo en cuenta la edad, las diferencias de mortalidad por nivel socioeconómico se observan en mujeres de 60 años en adelante (Figura 32).

Figura 32. Mortalidad por cáncer de mama por grupo de edad y quintil de privación para mujeres ≥ 30 años. Tasa específica por edad por 100.000 mujeres, escala logarítmica. España, 2011-2017.

