Jueves 22 de octubre 2020
FO-OS-226-20

Dr. Daniel Salas Peraza
Ministro
Ministerio de Salud de Costa Rica

Estimado Doctor,

Por este medio me permito saludarle y a su vez hacerle entrega formal del primer informe de investigación realizado por mi persona y el MSc. Romain Fantin. Este informe se basa sobre la primera publicación realizada con los datos del Registro de Tumores del Ministerio de Salud, cuyo proyecto se les presentó en el año 2019.

El título de esta primera investigación fue

"Gradiente social en la incidencia del cáncer en Costa Rica: Hallazgos del Registro Nacional de Tumores"

que permitió revelar la existencia de un gradiente social positivo entre la incidencia de cáncer y la posición socioeconómica de las personas, estimada según su distrito de residencia. Este proyecto hace parte de los objetivos del proyecto titulado "**Identificación y descripción de las inequidades sociales y territoriales del cáncer en Costa Rica"** inscrito en la Vicerrectoría de Investigación de la Universidad de Costa Rica (https://vinv.ucr.ac.cr/sigpro/web/projects/B9067) y cuyas unidades participantes fueron el Centro Centroamericano de Población, la Escuela de Salud Pública y la Facultad de Odontología de la Universidad de Costa Rica.

Este estudio permitió la publicación en la Revista ***Cancer Epidemiology***, titulada

"Social gradient in cancer incidence in Costa Rica:
Findings from a national population-based cancer registry"

que adjuntamos en el presente informe.

Agradeciéndole por su gran colaboración para la materialización de esta investigación, se despiden,

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Archivo

Informe de Investigación

Gradiente social en la incidencia del cáncer en Costa Rica:

Hallazgos del Registro Nacional de Tumores

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22/10/2020

Índice

1. Resumen

Antecedentes. La gran mayoría de la literatura concerniendo el estudio de las inequidades sociales en incidencia de cáncer proviene de países industrializados, aún cuando la OMS ha alertado sobre el impacto que estas podrían tener en los países de renta baja y media.

Objetivo. Analizar la asociación entre la incidencia de cáncer y la posición socioeconómica (PSE) en un país de ingresos medios (Costa Rica) entre 2011 y 2015.

Métodos. Se realizó un estudio ecológico a nivel de distrito electoral. Los 477 distritos del país se dividieron por área y nivel de riqueza según el censo de 2011. La muestra se definió utilizando los padrones electorales utilizados para las elecciones presidenciales de 2006 y 2010 (N = 2 798 517). Se incluyeron 44799 casos de cáncer provenientes del Registro de Cáncer de Costa Rica. Se utilizaron modelos de Cox para analizar la sobrevivencia.

Resultados. Todos los tipos de tumores combinados fueron incluidos en el análisis. Se observó un gradiente positivo, siendo la incidencia de cáncer menor en los distritos más desaventajados socioeconómicamente, comparados con los distritos más aventajados (HR_{Q2} = 0.98 [0.93–1.03], HR_{Q3} = 0.92 [0.85–0.99], HR_{Q4} = 0.83 [0,77-0,88]). Por sitio específico, para colon, piel, mama, próstata, tiroides y otros sitios de cáncer, se encontró un gradiente social positivo. Para los cánceres de estómago, pulmón y cuello uterino (invasivo o in situ), se encontró un gradiente social negativo. En el caso del cáncer de útero y linfoma (no Hodgkin), no se reveló una relación significativa entre nivel de riqueza del distrito e incidencia. Para el cáncer de piel, la incidencia fue mayor en las áreas rurales en comparación con las urbanas después de ajustar los modelos por el nivel de riqueza. En el caso del cáncer de pulmón, cuello uterino y útero, la incidencia fue menor en las zonas rurales en comparación con las zonas urbanas después del ajuste por nivel de riqueza.

Conclusiones. Los resultados mostraron que para todo tipo de cáncer combinados existe un gradiente social positivo, en el que la incidencia aumenta con el nivel de riqueza de los distritos. Este se encuentra en contradicción con la literatura internacional, pero confirmaron resultados de un estudio reciente en Costa Rica. Este estudio confirma la importancia de investigar las desigualdades socioeconómicas en países de ingresos medios, pues sus contextos sociales, así como la distribución de la prevalencia de los principales factores de riesgo del cáncer por estrato social, no es comparable con los países industrializados.

2. Introducción

Al analizar los determinantes sociales de la incidencia de cáncer en el mundo, se reportado la existencia de inequidades sociales en salud, tanto dentro, como, entre países. Para la mayoría de sitios específicos de cáncer investigados, una relación negativa del gradiente social se ha revelado: los grupos de individuos con mayor desventaja social son aquellos que poseen un mayor riesgo de padecer cáncer, en comparación los del medio de la jerarquía social, y estos últimos, a su vez, son más propensos en presentar un mayor riesgo de cáncer, que los que están en la cima de la jerarquía social (1–3). Los sitios de cáncer que se han encontrado asociados con una baja posición socioeconómica (PSE) son pulmón (4–9) tracto aerodigestivo (4,6,7,10), hígado (6,7), cervical (4) (4,6,7,10), estómago (6,10), esófago (6,10). Por el contrario, una ausencia de gradiente social o incluso un gradiente social positivo, donde una posición socioeconómica alta es asociada con una mayor incidencia, se han informado para cáncer de mama (4,6,10), próstata (4,6,10), piel (11), colon (12) y tiroides (6). Las explicaciones de estas desigualdades sociales en el cáncer son complejas e integran múltiples vías, tales como, estructuras sociales (por ejemplo, políticas públicas, acceso a los servicios de salud), factores socioeconómicos (por ejemplo, ingresos), condiciones de vida (por ejemplo, vivienda, hacinamiento, riesgos ocupacionales) y los comportamientos (consumo de tabaco, conductas sexuales de riesgo) (13). Todos estos elementos se relacionan con el grado de la desigualdad social en un país, materializada a través de una estructura política afectando finalmente la salud y la organización de los servicios de salud que pueden afectar de manera diferente a los grupos sociales en un país (14).

La relación entre la PSE y la incidencia de cáncer ha sido a menudo investigado a través de estudios ecológicos (15). Estos utilizan registros de cáncer poblacionales como principal fuente de datos. Así, se extrapola la PSE del lugar de residencia a la PSE del individuo. A menudo, se utilizan datos agregados provenientes de los censos, llamados indicadores de deprivación, para caracterizar los grupos sociales desde los más desaventajados hasta los más aventajados (15).

Sin embargo, la gran mayoría de esta evidencia científica proviene de países de ingresos altos, lo que ha dejado un vacío con respecto a las tendencias que se pueden observar en los países de renta baja y media. Sin embargo, se estima que las inequidades en salud en estos países representan uno de los principales problemas de salud pública.

Costa Rica es un país de renta media, cuyo ingreso per cápita es relativamente modesto (16), con respecto a países industrializados. Sin embargo posee indicadores de salud similares a los de los países de ingresos altos (17).

2.1. Objetivo

El objetivo de este estudio fue analizar la asociación entre la incidencia de cáncer en Costa Rica y la posición socioeconómica (PSE) entre 2011 y 2015, utilizando un enfoque ecológico.

2.2. Hipótesis

La incidencia de cáncer muestra un gradiente social negativo entre las poblaciones que habitan en los distritos más pobres (con mayor incidencia de cáncer), en comparación con aquellas que habitan en los distritos más ricos (con menor incidencia de cáncer).

3. Metodología

3.1. Descripción de la muestra.

La muestra se definió utilizando los padrones electorales utilizados para las elecciones presidenciales del 2006 y del 2010. Este incluye la lista de todos los ciudadanos costarricenses mayores de 18 años, que poseen un número de identificación único, denominado cédula. Debido a la importancia de la cédula en la vida cotidiana, la gran mayoría de los ciudadanos costarricenses están incluidos en los padrones electorales. Basados en información proveniente del Índice Nacional de Defunciones, las personas fallecidas antes del 1 de enero del 2011 fueron excluidos de los análisis. Los datos de los padrones electorales nacionales y el Índice Nacional de Defunciones del Registro Civil se fusionaron utilizando la cédula

Personas que no estaban inscritas en los padrones electorales ni en 2016 ni en 2018 se consideraron muertos antes de 2010 y, por lo tanto, excluidos de los análisis si no estaban en el Índice Nacional de Defunciones. La muestra final incluyó a 2 798 517 individuos.

3.2. Datos de cáncer.

El Registro del Cáncer de Costa Rica es un registro nacional creado en 1976 que enumera todos los casos de cáncer en el país [24]. El reporte al registro del cáncer es obligatorio para las instituciones de salud tanto públicas como privadas. El diagnóstico final es proporcionado posteriormente a un estudio clínico e histopatológico. Todos los casos diagnosticados entre el 1 de enero de 2011 y 31 de diciembre de 2015 fueron considerados en este estudio. Solo el primer cáncer registrado para cada paciente se incluyó. El Registro Nacional de Tumores de Costa Rica y el Registro de Defunciones del Registro Civil, se fusionó utilizando la cédula. Excluimos a los pacientes que no figuraban en el padrón electoral (mayoritariamente niños y extranjeros). Finalmente, se incluyeron 44799 casos de cáncer, lo que representa 1,6% de la muestra.

La décima revisión de la Clasificación Internacional de Enfermedades (ICD-10) se utilizó para definir el sitio del cáncer [28]. Los sitios comunes de cáncer se definieron como los que representan más del 2% del total de casos en el Registro de Tumores, que son sitios de cáncer con al menos 896 casos registrados: todos los cánceres combinados (44799 casos), estómago (ICD-10 C16, N = 3138), colon (ICD-10 C18, N = 2148), pulmón (ICD-10 C33-34, N = 998), piel no melanoma (ICD-10 C44, N = 10959), mama (mujeres) (ICD-10 C50, N = 5263), cuello uterino invasivo (ICD-10 C53, N = 1228), cuello uterino in situ (ICD-10 C53, N = 1564), útero (ICD-10 C54, N = 935), próstata (ICD-10 C61, N = 4490), tiroides (ICD-10 C73, N = 2721), linfoma no-Hodgkin (ICD- 10 C82-89, N = 944) y otros sitios de cáncer (10 411). Limitamos el análisis específico de los sitios de cáncer más comunes para garantizar la solidez de las estimaciones.

3.3. Datos socioeconómicos.

Se realizó un estudio ecológico a nivel del distrito electoral [29] referido siguiendo el Padrón Electoral. Caracterizamos los distritos usando el mismo enfoque utilizado anteriormente para estudiar la mortalidad por cáncer en Costa Rica [30]. Costa Rica, con 5 millones de habitantes, se divide administrativamente en 477 distritos (en 2015). Cada distrito se describió utilizando el censo de 2011.

El censo de 2011 incluye información individual anónima sobre más de 4,3 millones de personas (94% de la población en 2011). Los distritos fueron divididos por área (urbana, mixta y rural). La división por área está justificada por las diferencias significativas en el desarrollo y la ubicación de los y hospitales privados y establecimientos de salud entre urbanos, mixtos y zonas rurales (18). De hecho, como otros países latinoamericanos, las áreas rurales de Costa de Rica son más pobres y desfavorecidas en comparación con las urbanas (18). En las zonas rurales, los centros de atención oncológica están menos disponibles. Un distrito se considera urbano si más del 80% de su población vive en áreas urbanas, y rural si menos del 20% de su población vive en zonas urbanas [31]. Además, cada distrito se clasificó por su nivel de riqueza. El índice de riqueza utilizado fue el índice de Necesidades Básicas Insatisfechas (NBI), recolectado en el censo 2011(19). El NBI comprende cuatro dimensiones: acceso a una vivienda digna, acceso a una vida sana, (agua potable, desecho de excretas) acceso a la educación y acceso a otros bienes y servicios (19). Los distritos fueron divididos por NBI en cuartiles.

3.4. Modelos estadísticos.

Las tasas de incidencia estandarizadas por edad y sexo por 100 000 personas-año fueron estimados por área urbana / mixta / rural y por riqueza del distrito. La estandarización se basó en la distribución de la muestra global por sexo y edad quinquenal. Se utilizaron modelos de Cox. Estos nos permitieron tener en cuenta los riesgos competitivos existentes para la incidencia observada. Como resultado, personas que estaban vivas al comienzo del período de estudio y murieron antes del final del período de estudio sin tener cáncer se consideraron como censurados. Para el análisis de sitios específicos por cáncer, las personas se consideraron censuradas si tenían otro cáncer reportado anteriormente. El evento estudiado en los modelos de supervivencia fue el diagnóstico de cáncer. El tiempo de seguimiento comenzó el 1 de enero de 2011 y finalizó el 31 de diciembre de 2015. El índice de mortalidad del Registro Civil se utilizó para determinar la fecha de muerte de los individuos incluidos. Los modelos se ajustaron por sexo, edad al 1 de enero de 2011 y según las características socioeconómicas del distrito. La muestra final incluyó 13 832 524 años de seguimiento.

3.5. Datos y ética.

Este proyecto fue aprobado e inscrito por la Vicerrectoría de Investigación de la Universidad de Costa Rica según oficio (VI- 8126–2018).

4. Resultados

La Tabla 1 presenta las estadísticas descriptivas. La Tabla 2 presenta las tasas de incidencia estandarizadas por edad y sexo por área urbana / mixta / rural y riqueza. Para todos los sitios de cáncer combinados, mostrando un gradiente social positivo entre la incidencia de cáncer y riqueza: la incidencia disminuyó en los distritos más pobres (Q1 = 346,4 / 100.000 años-persona [340,8–351,9], Q2 = 337,6 [331,4–343,7], Q3 = 314,5 [308,4–320,6], Q4 = 285,7 [279,2–292,1]). Además, la incidencia de cáncer fue mayor en el área urbana (335,3 [331,4-339,2]), en comparación con el área mixta (302,7 [297,2–308,1]) y rural (320,2 [310,6-329,8]). Los análisis específicos de los sitios de cáncer más comunes revelaron claras diferencias. Para colon, mama, útero, próstata, tiroides y otros cánceres, se observó un claro gradiente social positivo, mientras que hubo un gradiente social negativo para el cáncer de estómago. De forma similar, la incidencia de cánceres de estómago y piel fue mayor en las zonas rurales en comparación con el área urbana, mientras que la incidencia de colon, pulmón, cáncer de mama, cervical, uterino, de próstata, de tiroides y otros fue mayor en zona urbana en comparación con zona rural.

La Tabla 3 presenta los resultados de los modelos de Cox para todos los sitios de cáncer, combinados y para cada sitio específico. Para todos los sitios de cáncer combinados, se confirmó el gradiente social positivo entre la incidencia de cáncer y riqueza. De hecho, la incidencia disminuyó en los distritos más pobres (HRQ2 = 0,98 [0,93–1,03], HRQ3 = 0,92 [0,85–0,99], HRQ4 = 0,83 [0,77–0,88]). Además, después del ajuste por riqueza, la incidencia de cáncer fue mayor en área rural en comparación con área urbana. Sin embargo, al excluir los cánceres de piel (no melanomas), la diferencia entre zonas urbanas y rurales desapareció. Los análisis específicos de los sitios de cáncer más comunes confirmaron las diferencias. Para colon, piel, mama, próstata, tiroides y otros sitios de cáncer, se observó un gradiente social positivo. Para estómago, pulmón, cáncer de cuello uterino (invasivo o in situ), un gradiente social negativo fue observado, siendo la incidencia mayor en los distritos más pobres que en el más rico. Para el cáncer de útero y el linfoma (no Hodgkin), no hubo una relación significativa entre riqueza e incidencia.

La asociación entre la incidencia del cáncer y el área urbana / rural también dependía de los sitios del cáncer. Para estómago, colon, mama, cuello uterino in situ, próstata, tiroides, linfoma y otros sitios de cáncer, no se encontró asociación significativa. Para el cáncer de piel, la incidencia fue mayor en las zonas rurales en comparación con las áreas urbanas (HR = 1,38 [1,15-1,66]). Para pulmón, cervical y cáncer de útero, la incidencia fue menor en las zonas rurales en comparación con las urbanas.

5. Conclusiones

La incidencia de cáncer mostró un gradiente social positivo para todos los sitios cancerosos en su conjunto. Este resultado fue similar al excluir la mayoría de sitios comunes de cáncer. El área rural tuvo una mayor incidencia de cáncer después de ajustar por la riqueza, sin embargo, esta diferencia desapareció al excluir el cáncer de piel.

Estos hallazgos están en contradicción con la literatura internacional, pero confirmó estudios previos realizados en Costa Rica. Al analizar el cáncer por sitio específico, las desigualdades socioeconómicas observadas fueron más coherentes con la literatura internacional. Las diferencias observadas entre nuestros resultados y la literatura internacional confirmaron la importancia de estudiar los aspectos socioeconómicos de la desigualdad social en Costa Rica y en países de ingresos medios en general. La etapa de desarrollo de cada país y el grado de impregnación de la cultura occidental moderna podría ser menos importante en algunos estratos de la sociedad, comparados a los países occidentales de ingresos altos, que podrían tener un efecto sobre la morbilidad. En este contexto, Costa Rica podría servir de ejemplo para la región. Costa Rica es un país de ingresos medios con una alta esperanza de vida, que desarrolló un conjunto de fuentes de datos excepcionales provenientes de censos, nacimientos, defunciones o registros de cáncer. Estos datos permitieron estudiar las desigualdades socioeconómicas en salud con precisión y podría permitir parcialmente encontrar nuevos determinantes de la salud.

6. Tablas

Table 1
Descriptive statistics of the sample. N = 2 798 517.

	Area			Wealth				Total
	Rural	Mixed	Urban	Q1	Q2	Q3	Q4	
Sex								
Men	148 879	419 354	827 114	392 766	356 957	336 973	308 651	1 395 347
Women	134 885	401 833	866 452	422 377	365 334	332 975	282 484	1 403 170
Cancer (N)	4 358	11 938	28 503	15 119	11 737	10 215	7 728	44 799

Table 2
Age-and-sex standardized incidence rate (per 100 000 person year). 13 832 524 person–years. N = 44 799 cancer diagnosed (all-cancer combined).

Variables	All cancer combined	Stomach (N = 3138)	Colon (N = 2148)	Lung (N = 1121)	Skin (N = 10 959)
Area					
Urban	335.3 [331.4–339.2]	21.9 [20.9–22.9]	16.8 [15.9–17.7]	8.0 [7.4–8.6]	77.7 [75.8–79.6]
Mixed	302.7 [297.2–308.1]	22.6 [21.1–24.1]	13.3 [12.1–14.4]	6.1 [5.3–6.9]	80.5 [77.7–83.4]
Rural	320.2 [310.6–329.8]	27.7 [24.9–30.4]	14.6 [12.6–16.7]	6.2 [4.9–7.5]	89.6 [84.5–94.7]
Wealth					
Q1 (richer)	346.4 [340.8–351.9]	20.5 [19.2–21.9]	17.9 [16.6–19.1]	7.1 [6.3–7.9]	80.0 [77.4–82.6]
Q2	337.6 [331.4–343.7]	23.3 [21.6–24.8]	17.8 [16.4–19.2]	7.3 [6.4–8.2]	88.5 [85.3–91.7]
Q3	314.5 [308.4–320.6]	23.0 [21.3–24.6]	13.3 [12.1–14.6]	8.0 [7.0–8.9]	77.8 [74.8–80.9]
Q4	285.7 [279.2–292.1]	25.4 [23.5–27.3]	11.6 [10.3–12.9]	6.5 [5.5–7.5]	70.6 [67.4–73.9]
Variables	Breast (N = 5263)[1]	Cervix (N = 1228) [1]	Cervix in situ (N = 1564) [1]	Uterus(N = 935) [1]	Prostate (N = 4490) [1]
Area					
Urban	80.6 [78.0–83.3]	18.1 [16.8–19.3]	22.1 [20.6–23.5]	14.2 [13.1–15.3]	69.9 [67.3–72.5]
Mixed	68.2 [64.5-72.0]	17.5 [15.6-19.3]	22.8 [20.7-24.9]	12.8 [11.2-14.5]	59.4 [56.1-62.7]
Rural	63.8 [57.4–70.1]	15.8 [12.8–18.9]	24.7 [21.0–28.4]	9.9 [7.4–12.4]	54.7 [49.5–60.0]
Wealth					
Q1 (richer)	88.8 [84.9–92.7]	16.1 [14.3–17.8]	18.1 [16.2–20.0]	14.6 [13.1–16.2]	72.3 [68.7–76.0]
Q2	74.4 [70.4-78.4]	17.3 [15.4-19.2]	24.3 [22.0-26.6]	13.0 [11.3-14.6]	69.5 [65.5-73.5]
Q3	71.5 [67.4–75.7]	20.4 [18.2–22.3]	24.4 [22.0–26.7]	13.3 [11.5–15.1]	61.7 [57.9–65.5]
Q4	59.7 [55.4–64.0]	17.8 [15.5–20.0]	24.6 [22.0–27.1]	12.1 (10.2–14.1]	53.8 [50.1–57.5]
Variables	Thyroid (N = 2721)	Lymphoma no Hodgkin (N = 944)	Other (N = 10 411)		
Area					
Urban	21.5 [20.6–22.5]	7.3 [6.7–7.9]	79.6 [77.7–81.5]		
Mixed	16.7 [15.5–18.0]	5.5 [4.8-6.3]	67.4 [64.8–70.0]		
Rural	16.4 [14.2–18.6]	7.5 [6.1–9.0]	73.5 [69.0-78.1]		
Wealth					
Q1 (richer)	25.2 [23.7–26.8]	7.5 [6.6-8.3]	83.1 [80.4–85.9]		
Q2	20.0 [18.6–21.5]	6.7 [5.9-7.6]	74.6 [71.8–77.5]		
Q3	16.4 [15.0–17.8]	6.4 [5.5–7.2]	73.9 [71.0–77.0]		
Q4	14.8 [13.3–16.2]	6.4 [5.5–7.4]	66.3 [63.2–69.3]		

Legend:Model adjusted for age, sex.[1]Breast, cervix and utero cancers incidence were calculated in women. Prostate cancers incidence was calculated in men.

Table 3
Cox model adjusted for area and district wealth. 13 832 524 person–years. N = 44 799 cancer diagnosed (all-cancer combined).

Variables	All cancer combined	Stomach (N = 3138)	Colon (N = 2148)	Lung (N = 1121)	Skin (N = 10 959)
Area					
Urban	1	1	1	1	1
Mixed	0.98 [0.92–1.05]	0.98 [0.86–1.10]	0.94 [0.83–1.07]	0.71 [0.59–0.85]	1.16 [0.98–1.36]
Rural	1.09 [1.01–1.17]	1.17 [0.99–1.39]	1.13 [0.94–1.35]	0.69 [0.52–0.92]	1.38 [1.15–1.66]
Wealth					
Q1 (richer)	1	1	1	1	1
Q2	0.98 [0.93–1.03]	1.13 [1.02–1.26]	1.01 [0.89–1.13]	1.09 [0.92–1.30]	1.08 [0.95–1.23]
Q3	0.92 [0.85–0.99]	1.11 [0.97–1.27]	0.75 [0.63–0.90]	1.29 [1.05–1.58]	0.91 [0.74–1.11]
Q4	0.83 [0.77–0.88]	1.19 [1.00–1.40]	0.64 [0.54–0.75]	1.21 [0.96-1.53]	0.74 [0.63–0.89]
Variables	Breast (N = 5263)	Cervix (N = 1228)	Cervix in situ (N = 1564)	Utero (N = 935)	Prostate (N = 4490)
Area					
Urban	1	1	1	1	1
Mixed	0.96 [0.90-1.03]	0.88 [0.76-1.03]	0.92 [0.70-1.21]	0.92 [0.77-1.09]	0.93 [0.83-1.03]
Rural	0.97 [0.86–1.10]	0.78 [0.61–0.99]	0.96 [0.74–1.25]	0.71 [0.52–0.96]	0.90 [0.78–1.03]
Wealth					
Q1 (richer)	1	1	1	1	1
Q2	0.85 [0.79–0.91]	1.11 [0.95–1.29]	1.36 [1.31–1.68]	0.90 [0.75–1.09]	0.98 [0.89–1.08]
Q3	0.82 [0.76–0.88]	1.34 [1.12–1.61]	1.38 [1.08–1.77]	0.95 [0.79–1.14]	0.88 [0.79–0.99]
Q4	0.69 [0.63–0.77]	1.25 [1.02–1.52]	1.42 [1.06–1.89]	0.94 [0.74–1.19]	0.80 [0.70–0.91]
Variables	Thyroid (N = 2721)	Lymphoma no Hodgkin (N = 944)	Other (N = 10 411)		
Area					
Urban	1	1	1		
Mixed	0.95 [0.83–1.09]	0.78 [0.65–0.93]	0.90 [0.83–0.98]		
Rural	1.03 [0.83–1.28]	1.03 [0.79–1.36]	1.02 [0.92–1.12]		
Wealth					
Q1 (richer)	1	1	1		
Q2	0.80 [0.70–0.92]	0.92 [0.77–1.11]	0.91 [0.85–0.98]		
Q3	0.66 [0.55–0.79]	0.91 [0.75–1.10]	0.92 [0.83–1.01]		
Q4	0.59 [0.50–0.70]	0.95 [0.73–1.23]	0.83 [0.76–0.91]		

Legend:Model adjusted for age, sex.

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8. Anexos: artículo científico publicado en Cancer Epidemiology en 2020

Título: *Social gradient in cancer incidence in Costa Rica: Findings from a national population-based cancer registry*

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Social gradient in cancer incidence in Costa Rica: Findings from a national population-based cancer registry

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ABSTRACT

Background: The main evidence regarding social inequalities in cancer risk comes from industrialized countries. The aim of this manuscript was to analyze the association between cancer incidence and socioeconomic position (SEP) in a middle-income country (Costa Rica) between 2011 and 2015.
Methods: An ecological study at the level of the electoral district was conducted. The 477 districts were divided by area and wealth using the 2011 Census. The sample was defined using the National Electoral Rolls used for presidential elections of 2006 and 2010 (N = 2 798 517). 44 799 cancer cases were included coming from the Costa Rican Cancer Registry. Cox models were used.
Results: All cancer sites combined, we observed a positive gradient, with incidence being lower in the poorest districts than in the wealthiest (HRQ2 = 0.98 [0.93 − 1.03], HRQ3 = 0.92 [0.85 − 0.99], HRQ4 = 0.83 [0.77 − 0.88]). For colon, skin, breast, prostate, thyroid and other cancer sites, a positive social gradient was observed. For stomach, lung, and cervical (invasive or in-situ) cancers, a negative social gradient was found. For uterine cancer and lymphoma (no-Hodgkin), there was no significant relationship between wealth and incidence. For skin cancer, incidence was higher in rural as compared to urban areas after adjustment for wealth. For lung, cervical and uterine cancer, incidence was lower in rural as compared to urban area after adjustment for wealth.
Conclusions: The all-cancer combined results were in contradiction with the international literature but confirmed recent study results in Costa Rica. It confirmed the importance of studying socioeconomic inequalities in middle-income countries.

1. Introduction

When analyzing the social determinants of all-cancer site incidence, health inequalities have been reported worldwide, both within and across countries [1]. For the majority of specific sites, a negative social gradient is revealed: the groups of individuals in the bottom of the social hierarchy are more likely to have a higher cancer risk, as compared to those on the middle, and the latter are in turn, more likely to present a higher cancer risk, than those at the top of the social hierarchy [1–3]. The cancer sites that have been found to be associated with low socioeconomic position (SEP) are lung [4–9], aerodigestive tract [4,6,7,10], liver [6,7], cervical [4,6,10,11] stomach [6,10], esophagus [6,10,12]. On the contrary, an absence of social gradient or even a positive social gradient, where a high socioeconomic position is associated with higher incidence, have been reported for breast [4,6,10,13], prostate [4,6,10,14], skin [4,6,10,15], colon [16], and thyroid [6]. The explanations to these social inequalities in cancer are complex, and integrate multiple pathways, such as, structural social factors (e.g. policies, access to health services), socioeconomic factors (e.g. income), living conditions (e.g. housing, overcrowding, occupational hazards), and the behavioral factors (e.g. tobacco, high-risk sexual behaviors) [17]. All of these elements relate to the degree of social inequality in a country, materialized through a political structure finally affecting both individual's health and health services organization [1].

The relationship between SEP and cancer incidence has been often studied with ecological studies that use population-based cancer registers as the main source of data. Based on this approach, the

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characteristics of the place of residence is used as a proxy of the individual socioeconomic position [6]. Area-level indicators that aggregate individual level measures of SEP (such as those coming from census data), can allow to create composite indicators of SEP, also known as "deprivation indices" [18,19]. These indices are widely used to allocate a deprivation score to each area in a country, that allows to range territories on a continuum from deprived to affluent [18].

The main evidence regarding social inequalities in cancer risk comes from industrialized countries [20]. However, according to the World Bank [21] and IARC [22] estimates, cancer incidence will represent the major burden of disease in Low and Middle Income Countries (LMICs), with over 20 million new cancer cases expected annually as early as 2025[21]. This phenomenon is mainly due to the global demographic and epidemiological transitions regarding life styles: tobacco consumption, infections, diet, reproductive, occupational, and environmental factors [17,21]. Ongoing surveillance of cancer incidence in LMICs is necessary, and yet, the majority of LMICs have poor quality data on cancer and limited cancer registers [23]. From that perspective, the study of the relationship between SEP and cancer incidence in LMICs, continues being a challenge for public health policies and interventions.

Costa Rica is a middle-income country which developed strategies to face this challenge. A national population-based cancer register was created in 1976, and achieved the nationwide coverage in 1980 [24]. Data comes from all public and private health services which have to make a mandatory notification of patients leaving their services with a diagnosis of cancer, as well as biopsy and autopsy reports with a cancer report form. The National Institute of Statistics and Census also have to make a mandatory notification of death certificates mentioning cancer [24]. In Costa Rica, after cardiovascular diseases, cancer is the second cause of death [25]. It is also one of the most unequal countries in the world according to a study ranking by the World Bank in 2016 [26]. On the other hand, Costa Rica has a national healthcare system, constitutionally conceptualized as universal, mandatory and solidary for all citizens [27]. This partially explains the country's good quality vital statistics, and a high life expectancy (80.2 years), similar to high income countries [27].

The aim of this manuscript was to analyze the association between cancer incidence in Costa Rica and socioeconomic position (SEP) between 2011 and 2015, using an ecological approach. The hypothesis tested was that cancer incidence showed a negative social gradient from those living in poorer districts (with higher cancer incidence), compared to those living in richer districts (with lower cancer incidence).

2. Materials and Methods

2.1. Sample

The sample was defined using the National Electoral Rolls used for presidential elections of 2006 and 2010. National Electoral Rolls included all Costa Rican citizens aged 18 years or older; all of them have a unique identification number, named *cédula*. Due to the importance of the *cédula* in the everyday life, the vast majority of Costa Rican citizens are included in the National Electoral Rolls. Based on information from the National Death Index, individuals deceased before January 1st, 2011 were excluded from the analyses. National electoral rolls and National Death Index were merged using the *cédula* identification number. People who were not enrolled in the National Electoral Rolls neither in 2016 nor in 2018 were considered dead before 2010 and therefore excluded from the analyses if they were not reported in the National Death Index.

The final sample included 2 798 517 individuals. Fig. 1 presents the flow-chart of the study.

2.2. Cancer data

Costa Rican Cancer Registry is a national population-based registry created in 1976 that lists all cancer cases in the country [24]. Reporting to the cancer registry is mandatory for public and private healthcare facilities. The final diagnosis of cancer is provided by a clinical and histopathological study. All cases diagnosed between January 1, 2011 and December 31, 2015 were included. Only the first registered cancer for each patient was included. Costa Rican Cancer Registry and National Death Index were merged using the *cédula*. We excluded patients who did not appear in the national electoral roll (mostly children and foreign people). Finally, 44 799 cancer cases were included, representing 1.6 % of the sample (Fig. 1). Sample characteristics are presented in Table 1.

The 10th revision of the International Classification of Diseases (ICD-10) was used to define cancer site [28]. The most common cancer sites were analyzed. Common cancer sites were defined as those representing more than 2% of the total cases in the Cancer Registry, that is cancer sites with at least 896 registered cases: all-cancer combined (44 799 cases), stomach (ICD-10 C16, N = 3138), colon (ICD-10 C18, N = 2148), lung (ICD-10 C33–34, N = 998), skin non-melanoma (ICD-10 C44, N = 10 959), breast (women) (ICD-10 C50, N = 5263), cervix invasive (ICD-10 C53, N = 1228), cervix in-situ (ICD-10 C53, N = 1564), uterus (ICD-10 C54, N = 935), prostate (ICD-10 C61, N = 4490), thyroid (ICD-10 C73, N = 2721), lymphoma no-Hodgkin (ICD-10 C82–89, N = 944), and other cancer sites (10 411). We limited the specific analysis to the most common cancer sites to ensure the robustness of the estimations.

2.3. Socioeconomic data

An ecological study at the level of the electoral district was conducted [29]. We characterized the districts using the same approach previously used to study cancer mortality in Costa Rica [30]. Costa Rica, with 5 million inhabitants, is administratively divided into 477 districts (in 2015). Each district was described using the 2011 Census. The 2011 Census includes anonymized individual information on more than 4.3 million people (94 % of the population in 2011). Districts were divided by area (urban, mixed, and rural). Division by area is justified by the significant differences in development and the location of public and private hospitals and health facilities between urban, mixed, and rural areas [29]. Indeed, as some other Latin American countries, Costa Rica's rural areas are poorer and underprivileged as compared to urban areas [29]. In rural areas, cancer care centers are less available, and services are often of poorer quality. A district is considered urban if more than 80 % of its population lives in urban areas, and rural if less than 20 % of its population lives in urban areas [31]. Additionally, the districts were classified by wealth. The percentage of people with at least one Basic Unmet Need (BUN) [32] is used by INEC and other Latin American statistical bureaus [33] to measure poverty at the geographical level. It comprises four dimensions: access to a decent shelter, access to a healthy life, access to knowledge and access to other goods and services. Districts were divided by BUN into quartiles of population according to the 2011 Census population in each district.

2.4. Model

Age-and-sex standardized incidence rates per 100 000 person-years were estimated by urban/mixed/rural area and by district's wealth (Table 2). The standardization was based on the distribution of the overall sample by sex and quinquennial age.

Cox models were used. Cox models allowed us to take into account the existing competitive risks to the observed incidence. As a result, people who were alive at the beginning of the study time period and died before the end of the study time period without having a cancer diagnosis were considered as censored. For specific analyses by cancer

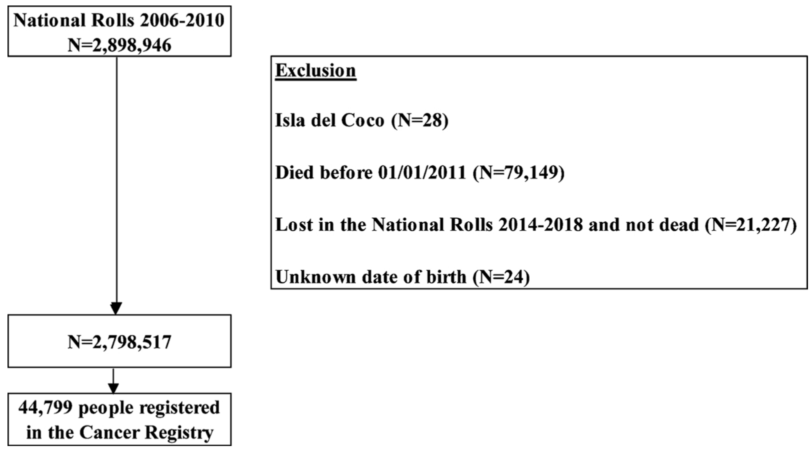

Fig. 1. Flow-chart (N = 2,798,517).

Table 1
Descriptive statistics of the sample. N = 2 798 517.

	Area			Wealth				Total
	Rural	Mixed	Urban	Q1	Q2	Q3	Q4	
Sex								
Men	148 879	419 354	827 114	392 766	356 957	336 973	308 651	1 395 347
Women	134 885	401 833	866 452	422 377	365 334	332 975	282 484	1 403 170
Cancer (N)	4 358	11 938	28 503	15 119	11 737	10 215	7 728	44 799

site, individuals were considered as censored if they had another cancer diagnosis besides the first incidence occurred during the study time period. Failure event was cancer diagnosis. Follow-up time started on January 1, 2011 and ended on December 31, 2015. The National Death Index was used to determine the date of death for individuals included in the sample.

Models were adjusted for sex, age on January 1, 2011, and district socioeconomic characteristics. The final sample included 13 832 524 years of follow-up. Cluster-robust standard errors were estimated

Table 2
Age-and-sex standardized incidence rate (per 100 000 person year). 13 832 524 person–years. N = 44 799 cancer diagnosed (all-cancer combined).

Variables	All cancer combined	Stomach (N = 3138)	Colon (N = 2148)	Lung (N = 1121)	Skin (N = 10 959)
Area					
Urban	335.3 [331.4–339.2]	21.9 [20.9–22.9]	16.8 [15.9–17.7]	8.0 [7.4–8.6]	77.7 [75.8–79.6]
Mixed	302.7 [297.2–308.1]	22.6 [21.1–24.1]	13.3 [12.1–14.4]	6.1 [5.3–6.9]	80.5 [77.7–83.4]
Rural	320.2 [310.6–329.8]	27.7 [24.9–30.4]	14.6 [12.6–16.7]	6.2 [4.9–7.5]	89.6 [84.5–94.7]
Wealth					
Q1 (richer)	346.4 [340.8–351.9]	20.5 [19.2–21.9]	17.9 [16.6–19.1]	7.1 [6.3–7.9]	80.0 [77.4–82.6]
Q2	337.6 [331.4–343.7]	23.3 [21.6–24.8]	17.8 [16.4–19.2]	7.3 [6.4–8.2]	88.5 [85.3–91.7]
Q3	314.5 [308.4–320.6]	23.0 [21.3–24.6]	13.3 [12.1–14.6]	8.0 [7.0–8.9]	77.8 [74.8–80.9]
Q4	285.7 [279.2–292.1]	25.4 [23.5–27.3]	11.6 [10.3–12.9]	6.5 [5.5–7.5]	70.6 [67.4–73.9]
Variables	Breast (N = 5263)[1]	Cervix (N = 1228) [1]	Cervix in situ (N = 1564) [1]	Uterus(N = 935) [1]	Prostate (N = 4490) [1]
Area					
Urban	80.6 [78.0–83.3]	18.1 [16.8–19.3]	22.1 [20.6–23.5]	14.2 [13.1–15.3]	69.9 [67.3–72.5]
Mixed	68.2 [64.5-72.0]	17.5 [15.6-19.3]	22.8 [20.7-24.9]	12.8 [11.2-14.5]	59.4 [56.1-62.7]
Rural	63.8 [57.4–70.1]	15.8 [12.8–18.9]	24.7 [21.0–28.4]	9.9 [7.4–12.4]	54.7 [49.5–60.0]
Wealth					
Q1 (richer)	88.8 [84.9–92.7]	16.1 [14.3–17.8]	18.1 [16.2–20.0]	14.6 [13.1–16.2]	72.3 [68.7–76.0]
Q2	74.4 [70.4-78.4]	17.3 [15.4-19.2]	24.3 [22.0-26.6]	13.0 [11.3-14.6]	69.5 [65.5-73.5]
Q3	71.5 [67.4–75.7]	20.4 [18.2–22.3]	24.4 [22.0–26.7]	13.3 [11.5–15.1]	61.7 [57.9–65.5]
Q4	59.7 [55.4–64.0]	17.8 [15.5–20.0]	24.6 [22.0–27.1]	12.1 (10.2–14.1]	53.8 [50.1–57.5]
Variables	Thyroid (N = 2721)	Lymphoma no Hodgkin (N = 944)	Other (N = 10 411)		
Area					
Urban	21.5 [20.6–22.5]	7.3 [6.7–7.9]	79.6 [77.7–81.5]		
Mixed	16.7 [15.5–18.0]	5.5 [4.8-6.3]	67.4 [64.8–70.0]		
Rural	16.4 [14.2–18.6]	7.5 [6.1–9.0]	73.5 |69.0-78.1]		
Wealth					
Q1 (richer)	25.2 [23.7–26.8]	7.5 [6.6-8.3]	83.1 [80.4–85.9]		
Q2	20.0 [18.6–21.5]	6.7 [5.9-7.6]	74.6 [71.8–77.5]		
Q3	16.4 [15.0–17.8]	6.4 [5.5–7.2]	73.9 [71.0–77.0]		
Q4	14.8 [13.3–16.2]	6.4 [5.5–7.4]	66.3 [63.2–69.3]		

Legend:Model adjusted for age, sex.[1]Breast, cervix and utero cancers incidence were calculated in women. Prostate cancers incidence was calculated in men.

2.5. Sensitivity analysis

A sensitivity analysis was conducted by modeling a multilevel mixed-effects Poisson regression [30]. The outcome variable was the number of diagnosed cancers for each quinquennial age, sex and district. The population denominator was the number of years of follow-up for each quinquennial age, sex and district. Incidence-rate ratios (IRR) are available in Supplementary materials. Models were adjusted for age, sex, and district's characteristics.

2.6. Ethical approval

Ethics approval was provided by the Universidad de Costa Rica (VI-8126–2018).

3. Results

Table 2 presents the age-and-sex standardized incidence rates by urban/mixed/rural area and wealth. For all-cancer sites combined, there was a positive social gradient between cancer incidence and wealth. Indeed, incidence decreased in poorer districts (Q1 = 346.4/100,000 person-years [340.8 – 351.9], Q2 = 337.6 [331.4 – 343.7], Q3 = 314.5 [308.4 – 320.6], Q4 = 285.7 [279.2 – 292.1]). Moreover, cancer incidence was higher in urban area (335.3 [331.4 – 339.2]) as compared to mixed (302.7 [297.2 – 308.1]) and rural area (320.2 [310.6 – 329.8]). The specific analyses of the most common cancer sites revealed clear differences. For colon, breast, uterine, prostate, thyroid and other cancers, a clear positive social gradient was observed, whereas there was a negative social gradient for stomach cancer. Similarly, the incidence of stomach and skin cancers was higher in rural area as compared to urban area, whereas the incidence of colon, lung, breast, cervical, uterine, prostate, thyroid, and other cancers was higher in urban area as compared to rural area.

Table 3 presents the results of the Cox models all-cancer sites combined and for each cancer site. For all-cancer sites combined, it confirmed the positive social gradient between cancer incidence and wealth. Indeed, incidence decreased in poorer districts (HR_{Q2} = 0.98 [0.93–1.03], HR_{Q3} = 0.92 [0.85–0.99], HR_{Q4} = 0.83 [0.77–0.88]). Moreover, after adjustment for wealth, cancer incidence was higher in rural area compared to urban area. Nevertheless, when excluding non-melanoma skin cancer, the difference between urban and rural areas disappeared.

The specific analyses of the most common cancer sites confirmed clear differences. For colon, skin, breast, prostate, thyroid and other cancer sites, a positive social gradient was observed. For stomach, lung, and cervical (invasive or in-situ) cancers, a negative social gradient was observed, with incidence being higher in the poorest districts than in the wealthiest. For uterine cancer and lymphoma (no-Hodgkin), there was no significant relationship between wealth and incidence.

Association between cancer incidence and urban/rural area also depended on cancer sites. For stomach, colon, breast, cervix in-situ, prostate, thyroid, lymphoma, and other cancer sites, no significant association was found. For skin cancer, incidence was higher in rural as compared to urban areas (HR = 1.38 [1.15–1.66]). For lung, cervical and uterine cancer, incidence was lower in rural as compared to urban area.

The sensitivity analysis conducted by modeling a Poisson regression yielded remarkably similar results (see Supplementary materials).

4. Discussion

Cancer incidence followed a positive social gradient for all-cancer-sites combined. This result remained similar when excluding the most common cancer sites. Rural area had higher cancer incidence after adjustment for wealth, however this difference disappeared when excluding skin cancer. The relationship between socioeconomic position and cancer incidence, as well as the relationship between urban/rural area and cancer incidence, varied according to the cancer site.

The all-cancer-sites combined results were not in line with the international literature on high-income countries [1,2], or even with

Table 3
Cox model adjusted for area and district wealth. 13 832 524 person–years. N = 44 799 cancer diagnosed (all-cancer combined).

Variables	All cancer combined	Stomach (N = 3138)	Colon (N = 2148)	Lung (N = 1121)	Skin (N = 10 959)
Area					
Urban	1	1	1	1	1
Mixed	0.98 [0.92–1.05]	0.98 [0.86–1.10]	0.94 [0.83–1.07]	0.71 [0.59–0.85]	1.16 [0.98–1.36]
Rural	1.09 [1.01–1.17]	1.17 [0.99–1.39]	1.13 [0.94–1.35]	0.69 [0.52–0.92]	1.38 [1.15–1.66]
Wealth					
Q1 (richer)	1	1	1	1	1
Q2	0.98 [0.93–1.03]	1.13 [1.02–1.26]	1.01 [0.89–1.13]	1.09 [0.92–1.30]	1.08 [0.95–1.23]
Q3	0.92 [0.85–0.99]	1.11 [0.97–1.27]	0.75 [0.63–0.90]	1.29 [1.05–1.58]	0.91 [0.74–1.11]
Q4	0.83 [0.77–0.88]	1.19 [1.00–1.40]	0.64 [0.54–0.75]	1.21 [0.96-1.53]	0.74 [0.63–0.89]
Variables	Breast (N = 5263)	Cervix (N = 1228)	Cervix in situ (N = 1564)	Utero (N = 935)	Prostate (N = 4490)
Area					
Urban	1	1	1	1	1
Mixed	0.96 [0.90-1.03]	0.88 [0.76-1.03]	0.92 [0.70-1.21]	0.92 [0.77-1.09]	0.93 [0.83-1.03]
Rural	0.97 [0.86–1.10]	0.78 [0.61–0.99]	0.96 [0.74–1.25]	0.71 [0.52–0.96]	0.90 [0.78–1.03]
Wealth					
Q1 (richer)	1	1	1	1	1
Q2	0.85 [0.79–0.91]	1.11 [0.95–1.29]	1.36 [1.31–1.68]	0.90 [0.75–1.09]	0.98 [0.89–1.08]
Q3	0.82 [0.76–0.88]	1.34 [1.12–1.61]	1.38 [1.08–1.77]	0.95 [0.79–1.14]	0.88 [0.79–0.99]
Q4	0.69 [0.63–0.77]	1.25 [1.02–1.52]	1.42 [1.06–1.89]	0.94 [0.74–1.19]	0.80 [0.70–0.91]
Variables	Thyroid (N = 2721)	Lymphoma no Hodgkin (N = 944)	Other (N = 10 411)		
Area					
Urban	1	1	1		
Mixed	0.95 [0.83–1.09]	0.78 [0.65–0.93]	0.90 [0.83–0.98]		
Rural	1.03 [0.83–1.28]	1.03 [0.79–1.36]	1.02 [0.92–1.12]		
Wealth					
Q1 (richer)	1	1	1		
Q2	0.80 [0.70–0.92]	0.92 [0.77–1.11]	0.91 [0.85–0.98]		
Q3	0.66 [0.55–0.79]	0.91 [0.75–1.10]	0.92 [0.83–1.01]		
Q4	0.59 [0.50–0.70]	0.95 [0.73–1.23]	0.83 [0.76–0.91]		

Legend:Model adjusted for age, sex.

results in middle-income countries such as Chile [3]. Nevertheless, they were consistent with national literature. Cancer incidence was found to be associated with a higher socioeconomic position in Costa Rica, in opposition with what has been described elsewhere [34]. This association remained significant even after excluding the most common cancer sites from the analysis. This study results were consistent with those of a study conducted in Costa Rica in the nineties. Wesseling et al. showed that, with no adjustment for wealth, the incidence of most of cancer sites was higher in urban as compared to rural areas [35]. Given that rural areas are significantly poorer than urban areas [29], this study results are along the same lines of Wesseling and colleagues' results. Indeed, we found a similar results before adjustment for wealth. Moreover, we recently demonstrated that higher cancer mortality was associated with high socioeconomic position for all-cancer-sites combined [30]. This positive social gradient is surprising, nevertheless Singh et al., found similar results in United States a few decades ago [36], and some similar findings were revealed in East-European countries in the nineties [34]. This might be due to the distribution of common risk factors in Costa Rica. Indeed, in high-income countries, obesity, smoking or alcohol are usually associated with low socioeconomic position [37]. In Costa Rica, prevalence of tobacco smoking is low and associated with urban area but only slightly associated with socioeconomic indicators [38]. Alcohol consumption is strongly associated with high socioeconomic position [39]. There are contradictory results linking obesity and socioeconomic position [40,41]. More studies on the link between economic position and cancer risk factors in Costa Rica are needed to better understand our results. Finally, earlier cancer diagnoses in the richest districts can also be suggested as a hypothesis to be explored.

The specific analyses by cancer sites were more consistent with international literature. Indeed, both at the international level and in our study, breast, prostate, non-melanoma skin, colon, and thyroid cancer, in a number of studies and countries [4,6,9,13–16] including LMICs [3,42] have shown, either an absence or a positive social gradient. Along the same lines, stomach, lung, and cervical cancer showed a negative social gradient both in our study and in the international literature [4–9,11], including LMICs [3,43]. The fact that specific analyses by cancer sites were consistent with the international literature whereas analysis of all-cancer combined (even after excluding most common cancer sites) was not, can be due to the relative weakness of the negative social gradient we observed in particular for lung cancer [4,8].

Our results were not fully consistent with our previous study on cancer mortality, even if the trends were similar [30]. Indeed, both for mortality and incidence, we found a positive social gradient for colon, skin, breast, prostate cancer, and a negative social gradient for cervical cancer. Nevertheless, for lung and stomach cancer, no significant association with wealth had been found for mortality, but it has now been found for incidence. Also, for lymphoma, a positive social gradient had been found for mortality, but now it has not been found for incidence. We found a negative social gradient for stomach and lung cancers in incidence, whereas it was not significant in mortality. Further analyses are needed to understand the differences between the two studies. It might be due to various factors: we used different databases, coming from different institutions in the two studies; the incidence model took into account the mortality due to other causes; mortality study involved estimations of the district populations; incidence and mortality might have different risk factors due to survival and deaths involving various causes; the measure of the district of residence was different; the studied period was slightly different.

There was no relation between area and cancer incidence for the majority of cancer sites. Skin cancer incidence was higher in rural area. This might be due to the highest proportion of outdoor workers in rural area. Lung cancer incidence was higher in urban areas, which was consistent with the highest prevalence of tobacco use in urban areas [38]. Cervical and uterine cancer was higher in urban area, which was also consistent with previous studies in LMICs [44,45].

Our study had some weaknesses. We excluded children and foreign people. A sub-registration of some cases might exist, in particular for early stage cancers. For example, significantly higher increases in incidence in the most disadvantaged populations were observed in the studied period. Since the Costa Rican health system is excellent and free, the existence of a massive sub-registry seems unlikely. We used the electoral district, which is defined in Costa Rica using the official residence, and might be different from the real residence. For example, some districts had more population in the electoral rolls compared to data from the 2011 Census or official estimations. Nevertheless, the electoral district was defined before the cancer diagnosis, which avoids the risk of information bias. In the absence of data at the individual level, we implemented an ecological study using the individual data aggregated at the level of geographic units. The results of an ecological study are not necessarily fully transferable at the individual level. Nevertheless, we have been able to describe places of residence with great precision, since Costa Rica had nearly 500 districts and we relied on census data. 4.3 million of people representing 94 % of the population in 2011 participated to the census which ensured the quality of the data at the district level.

Our study had several strengths. The main one is the design. Merging the National Electoral Rolls and the National Cancer Registry with the cédula, we were able to follow a sample of more than 2 798 000 people during five years. As a result, we did not need to use estimations of the population of each district, which have a great advantage and eliminate bias possibilities. Moreover, the use of a national cancer registry, instead of a regional one, limited the loss of cases. We were able to count on more than 44 000 cases of diagnosed cancers, which allowed us to study specifically 11 different cancer sites. Reporting cancer cases to the registry is mandatory in Costa Rica and the final diagnoses of cancer are provided by a clinical and histopathological study, which assured the quality of the data. To the best of our knowledge, there are very few similar studies relating socioeconomic position and cancer incidence for a large range of cancer sites in low- or middle-income countries.

Our study showed a positive social gradient for all-cancer-sites combined incidence. It was in contradiction with the international literature but it confirmed recent study results in Costa Rica. When analyzing by cancer site, the observed socioeconomic inequalities were more consistent with international literature and slightly different from our previous study. The observed differences between our results and the international literature confirmed the importance of studying socioeconomic inequalities in Costa Rica and in middle-income countries in general. The stage of development and the impregnation of the modern occidental culture is less important in some stratum of the society than in occidental high-income countries, which might have an effect on morbidity. In this context, Costa Rica might have a role. Costa Rica is a middle-income country with a high life-expectancy, which developed exceptional datasets coming from census, birth, death or cancer registries. These datasets allowed studying socioeconomic inequalities in health with precision. It might partially allow finding new determinants of health.

Authorship contribution

Romain Fantin:conception, design, acquisition of data, analysis, interpretation of data, redaction

Carolina Santamaría Ulloa: interpretation of data, redaction

Cristina Barboza Solís: acquisition of data, interpretation of data, redaction

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CRediT authorship contribution statement

Romain Fantin: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing. **Carolina Santamaría Ulloa:** Investigation, Methodology, Writing - original draft, Writing - review & editing. **Cristina Barboza Solís:** Investigation, Methodology, Resources, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2020.101789.

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