TESIS DOCTORAL

ATENCION INTEGRADA EN LA ENFERMEDAD PULMONAR OBSTRUCTIVA CRONICA

Memoria de tesis presentada por
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para obtener el título de
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DEDICATORIA

A María Constanza, el motor de mis sueños

A Juliana, Emilia y Rafael, los motores de mi vida
A la memoria de mi padre: su sueño inspiró mi vida

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Durante mi formación profesional como especialista en medicina interna y neumología en la Universidad Javeriana de Bogotá, siempre tuve la ilusión de involucrarme temporalmente en un grupo de investigación clínica sólido y reconocido, que me aportara las herramientas necesarias para fortalecer y consolidar mis conocimientos alrededor de esta disciplina.

Con el estímulo personal y académico de mi maestro el doctor Darío Maldonado y el beneplácito de mi institución madre la Fundación Neumológica Colombiana, en el año 1999 y gracias a un ofrecimiento del profesor Roberto Rodríguez-Roisin y al apoyo incondicional de mi esposa María Constanza, pude involucrarme como becario de investigación del proyecto CHRONIC de la Unión Europea. Este proyecto era liderado por el profesor Josep Roca del Hospital Clínic de Barcelona, la institución española de mayor prestigio en este campo. La beca, que inicialmente fue otorgada para dos años, fue posteriormente ampliada por dos más durante el desarrollo del proyecto, lo que me permitió completar mis estudios de doctorado y desarrollar los trabajos descritos en esta tesis.

Fueron cuatro años muy difíciles, pero a su vez los más fructíferos de mi vida profesional y académica. Crecí, desarrollé destrezas y forjé habilidades que desconocía tener, y aprendí que lo más importante para desarrollarse esta en uno mismo, como lo dice el proverbio catalán “tu mateix” o “hazlo tú mismo”. Amplié mis conocimientos en disciplinas vitales para entender la cultura de la investigación y sobre todo comprendí la importancia de trabajar en equipo con diferentes profesionales.

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Mi sentimiento de gratitud y amistad para todos aquellos que participaron o tuvieron que ver con esta tesis:

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A Myriam, fiel compañera de escritorio. Por su interés en ver terminado mi proyecto y su prudencia y ternura para con mi familia; a ella, mi admiración y cariño.

A Joan Albert, Felip, Conchi, Carme, Maite, José Luis y Tere, el corazón del laboratorio de función pulmonar, escalera 3B sótano, por el afecto que han profesado siempre hacia mí y hacia mi familia.

A todos los socios del proyecto CHRONIC que permitieron alcanzar los resultados esperados.

A Juan y Marce, mi familia en Barcelona y la que me heredaron en Bogotá. Sin ellos todo hubiera sido muy distinto. Las charlas y confesiones con Juan, los niños, y los cuidados de Marce fueron mi apoyo durante todo este proceso.

A mi madre, que falleció durante mi estancia en Barcelona, todo mi amor. Me queda su empuje y valentía para no dejarse vencer por las dificultades. “Regia” con María Constanza y adorable con mis hijas.

A Carlos Alberto mi hermano y mejor amigo, porque así le cueste creo que él me entiende y me conoce muy bien. El mejor tío para mis hijos; gracias por no descuidar a mi familia durante mis ausencias.

A mis hermanas Marisa, Marti y Nandita porque a pesar de la distancia se que nunca dejaron de interesarse en mis progresos, animándome para no desfallecer.

A mis tíos paternos Carmen, Clara, Soledad, Pedro, Hernando e Isabel a quienes les debo el espíritu educador que acompaña mi vida profesional y el amor por mis costumbres y por mi patria, que tanta falta me hicieron durante mis años de ausencia.

A todos y cada uno de ellos, mi GRATITUD SIEMPRE!

PRESENTACIÓN

La presentación de esta tesis doctoral se realiza en forma de compendio de artículos publicados según la normativa aprobada por la Comisión de Doctorado de la Universidad de Barcelona. En la introducción se detallan los aspectos que condicionan un aumento en la prevalencia de las enfermedades crónicas como la EPOC y la eficacia limitada de los sistemas sanitarios actuales para gestionar el cuidado de los pacientes con episodios de exacerbación. El planteamiento de un nuevo paradigma para la atención de estos pacientes justifica la hipótesis de trabajo de esta tesis. El núcleo de la tesis lo constituyen cinco manuscritos originales, cuatro de ellos ya publicados en revistas internacionales de alto impacto y uno de ellos enviado para publicación. Todos los artículos pertenecen a una misma línea de investigación, inspirados en el proyecto CHRONIC[I] , que fue concebido para desarrollar estrategias en el domicilio del paciente fundamentadas en un nuevo modelo de atención integrada propuesto. En los manuscritos 1, 2 y 3 se centra la atención en la implementación de este tipo de estrategias para la gestión aguda de los episodios de exacerbación, mientras los manuscritos 4 y 5 se desarrollaron para prevenir la aparición de nuevos episodios de exacerbación. En el anexo de la presente tesis se incluye la editorial realizada por los Dres. Seemungal T.A.A.R. y Wedzicha J.A. que mereció el cuarto manuscrito de la tesis, publicado en el European Respiratory Journal[II]. Considero que este material ayuda a contextualizar la presente tesis en el debate existente sobre los nuevos modelos de atención sanitaria para las exacerbaciones de EPOC.

[I] CHRONIC project. An information capture and processing environment for chronic patients in the information society. V pro gram of the European Union, DG XIII, IST-1999/12158.

[II] Seemungal T.A.R., Wedzicha J.A. Integrated care: a new model for COPD management? Eur Respir J 2006; 28: 4–6

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INTRODUCCION

El Cambio Demográfico y la Salud

Las interacciones entre sociedad y salud tienen una importancia indudable, desde diversas perspectivas. El papel emergente de las enfermedades crónicas que se incrementará en las próximas décadas, exigirá replantear y estructurar nuevos procesos de transición en las relaciones salud-sociedad. La presente tesis doctoral tiene su justificación en la necesidad de adaptar los sistemas sanitarios a esta nueva realidad.

A lo largo de la historia, las enfermedades han tenido una marcada influencia sobre los cambios demográficos, económicos y sociológicos de nuestras sociedades, y a su vez esos cambios sociales han generado un gran impacto sobre la salud pública[1]. Esta estrecha interrelación, conocida como transición demográfica, se puede entender mejor a través de los cambios observados en la dinámica poblacional Europea. Mientras que los siglos XIX y primera mitad del siglo XX se caracterizaron por elevadas tasas de mortalidad y fecundidad con una baja esperanza de vida al nacer, en la actualidad observamos un notable decrecimiento de ambas tasas y un extraordinario crecimiento poblacional condicionado por una mayor esperanza de vida, propias de sociedades industrializadas y con un mayor crecimiento económico[2](figura 1).

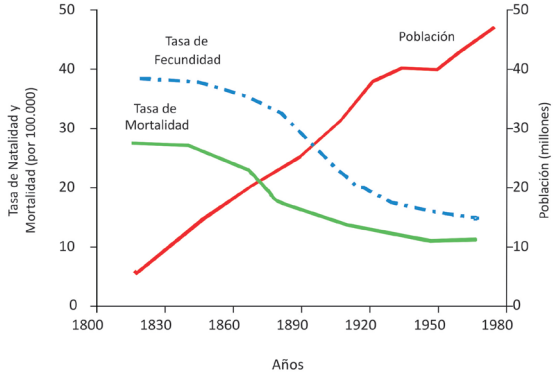

Figura 1: Modelo de transición demográfica en Inglaterra y Gales entre 1800 a 1980. Se observa que las tasas de fecundidad y mortalidad cayeron durante casi dos siglos, con un incremento progresivo de la población solo atenuado cuando la tasa de fecundidad se aproximó a la de mortalidad[1].

A esta tendencia demográfica general, se asoció el aumento progresivo de la mortalidad por enfermedades crónicas, que se situó por encima de las infecciosas desde la década de los 1970s en los países desarrollados[3] (figura 2). Los determinantes más importantes de este cambio posiblemente fueron:

- Factores eco-biológicos relacionados con un balance entre los agentes infecciosos, el nivel de hostilidad del ambiente y la resistencia del huésped.

- La adopción de hábitos nocivos y estilos de vida poco saludables (tabaquismo, vida sedentaria, alimentación no equilibrada, altos niveles de estrés, etc.).

- Los sistemas sanitarios, que definen las políticas necesarias para prevenir y gestionar el tratamiento de las enfermedades, tanto a nivel individual como a nivel poblacional[1;4;5].

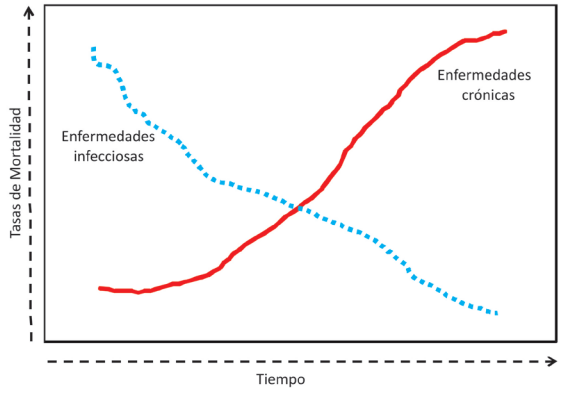

Figura 2: Cambio en la tendencia demográfica por tasas de mortalidad entre las enfermedades infecciosas y las crónicas, en países desarrollados[6].

Estos fenómenos demográficos y epidemiológicos, que juegan un rol significativo sobre los cambios culturales y sociales asociados con la salud de las poblaciones, se acuñan bajo el término de transición de la salud[7]. Con este concepto, se reconoce que el buen estado de salud poblacional dependerá de los mismos individuos, de los avances en las ciencias de la salud y de la capacidad de gestión de los servicios sanitarios para desplegar intervenciones adecuadas a gran escala[6;8].

Epidemiología poblacional

Los cambios referidos han contribuido de forma determinante al aumento de la esperanza de vida de la población en los países desarrollados. Si para el quinquenio 2000-2005 era de 76 años, se estima que en el 2050 alcanzará los 81 años, siendo unos cinco años superior en mujeres que en hombres[9]. El crecimiento de la población mayor de 65 años es extraordinariamente importante. Si para 1950 el porcentaje de sujetos mayores de 65

años con respecto a la población total era del 8%, se estima que con una tasa anual de crecimiento del 2.8% hasta el año 2030, este porcentaje aumentará al 21.4% (unos 2000 millones de personas) en el 2050[10](figura 3).

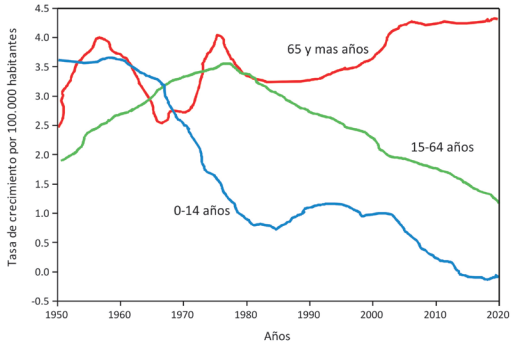

Figura 3: Crecimiento de la población por grupos de edad a través de los años, expresado como tasa por 100.000 habitantes. Solamente en la población de 65 años o más se observa un crecimiento sostenido[10].

Para dicho año y por primera vez en la historia de la humanidad, el número de personas mayores será muy semejante al de los niños y adolescentes, como se refleja en las pirámides poblacionales[11](figura 4).

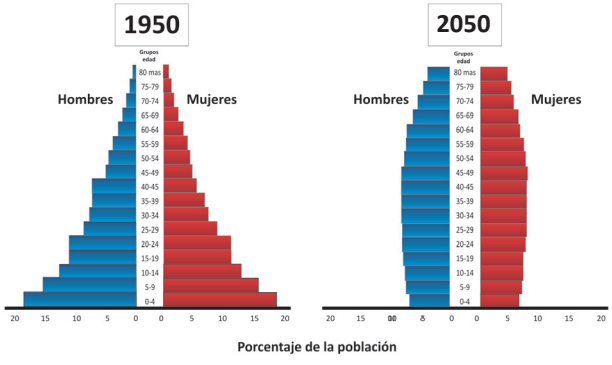

Figura 4: Porcentaje de la población por grupos de edad y sexo a nivel mundial en 1950 (izquierda) y el estimado para 2050 (derecha). La pirámide poblacional esperada para el año 2050 muestra una disminución de los grupos más jóvenes (principalmente los menores de 15 años) y un aumento de la población en edades laborales y adultos mayores[11].

Todos estos cambios, también han generado un mayor gasto en salud, que se ha venido incrementando a un ritmo mayor que el crecimiento económico general. De acuerdo con los cálculo estimados, los países de la Organización para la Cooperación y el Desarrollo Económicos (OCDE) dedicaron en el 2003 un promedio del 8.8% de su producto interno bruto (PIB) al gasto en salud, frente al 7.1% en 1990 y al 5% en 1970. Sin embargo solo el 3% del gasto se dedica a la prevención y a programas de salud pública[12].

El envejecimiento también tendrá repercusiones significativas en el ámbito social. Al disminuir la población económicamente activa, el número de personas en edad de trabajar por cada persona mayor de 65 años, pasará de 9 en la actualidad a 4 o menos a mitad de siglo y el acompañamiento familiar hacia los mayores será menor. Además, afectará los regímenes de pensiones y las aportaciones de la población activa a la seguridad social[10]. Todos estos aspectos generarán un fenómeno de exclusión y aislamiento social cada vez más acentuados, por lo que se presume que los servicios de soporte social serán cada vez menos accesibles[13].

Enfermedades crónicas: epidemiología e impacto

Las enfermedades crónicas han sido definidas como padecimientos que persisten por períodos prolongados de tiempo, con etiología multifactorial y curso clínico tortuoso caracterizado por episodios de recaídas o exacerbaciones que generan disfunciones en los sistemas sanitarios y una elevada utilización de recurso. Frecuentemente son incurables y producen discapacidad funcional y dependencia de gran impacto social y económico para las sociedades modernas[14]. Las de mayor impacto son las enfermedades cardíacas y cerebro-vasculares, las respiratorias crónicas, la diabetes, la obesidad, el cáncer y los trastornos depresivos[9]. Se ha estimado que unas 100 millones de personas en el mundo murieron por enfermedades relacionadas con el tabaco en el siglo XX, cifra que puede aumentar a 1 billón al final del siglo XXI, de acuerdo con las predicciones[15;16].

El riesgo de padecerlas incrementa con la edad y se prevé que su prevalencia aumente progresivamente en las próximas décadas[17]. En el año 2005, se estimó que un 21% de los norteamericanos tenía al menos una condición crónica, y uno de cada tres sujetos mayores de 65 años tenía más de una de ellas[18]. Para el mismo año, los cálculos de la Organización Mundial de la Salud (OMS) revelaron un total de 58 millones de defunciones por todas las causas, siendo un 60,3% debidas a enfermedades crónicas, el doble de las catalogadas como no crónicas[19](figura 5).

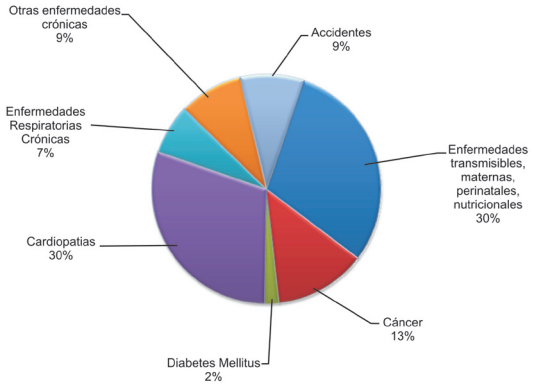

Figura 5: Distribución de las principales causas de mortalidad por grupos de enfermedades, de un total de 58 millones de muertes para el 2005[19].

Las enfermedades crónicas representan el 72% de la carga global de todas las enfermedades en los sujetos mayores de 30 años[19]. La carga de la enfermedad se determina al medir los años de vida saludable (AVISAs) que pierde una población por muerte o discapacidad. Los AVISAs entre lo observado en 1990 y lo esperado para el 2020, muestran como el impacto por patologías crónicas se duplicará comparativamente con los de las enfermedades trasmisibles, maternas, perinatales y por deficiencias nutricionales, que pasará a ser la mitad[20](figura 6).

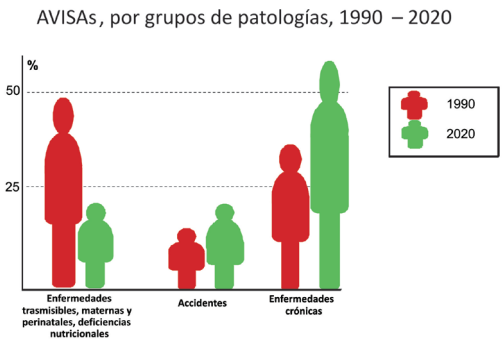

Figura 6: Impacto de los AVISAs por grupos de patologías entre 1990 y 2020. Sugiere que las patologías crónicas se duplicarán mientras que el grupo de enfermedades trasmisibles, maternas y perinatales y las relacionadas con deficiencias nutricionales pasará a ser la mitad en países en vías de desarrollo[20].

Los perfiles de disminución de prevalencia de algunas de estas enfermedades crónicas (i.e cardiovasculares) en los países desarrollados son indicativos del potencial existente para conseguir una prevención efectiva. Cabe señalar que si bien las enfermedades cardiovasculares representaron aproximadamente el 20% del total de las AVISAs, es conocido que al menos dos terceras parte de ellas pudieron haber sido evitadas con estilos de vida más saludables (por ejemplo, actividad física regular, dieta equilibrada y evitar la exposición al tabaco[21]). Además, el impacto sobre los gastos anuales en salud de un paciente con enfermedad crónica, puede llegar a ser cinco veces más alto que los de una persona sana, y aumentar en más del doble por cada condición comórbida adicional[18;22].

Para el 2005 la OMS planteó la necesidad de implementar estrategias a gran escala, con el objetivo de disminuir la carga global de las enfermedades crónicas en un 2% cada año hasta el 2015, lo que podría evitar unas 36 millones de defunciones en el mundo durante este período[23]. Desde el punto de vista preventivo estas estrategias deberían enfocarse en modificar los hábitos de comportamiento y los factores de riesgo de poblaciones específicas, y desde el punto de vista terapéutico en modular y modificar el curso de las enfermedades[14]. Estas iniciativas seguramente recogerán los frutos de otras estrategias preventivas de la OMS como el Convenio Marco para el Control del Tabaco[24] y la Estrategia Mundial sobre Régimen Alimentario, Actividad Física y Salud[25]. Las estrategias públicas a gran escala, determinarán en gran parte, la forma como los sistemas sanitarios deberán abordar la gestión de las enfermedades crónicas.

La EPOC: una enfermedad respiratoría crónica con un fuerte impacto sanitario

Definición y epidemiología

La Enfermedad Pulmonar Obstructiva Crónica (EPOC) es reconocida como la patología respiratoria asociada a inhalación de gases tóxicos (tabaco y/o ambientales) de mayor impacto sobre la salud en sujetos mayores, aun cuando cada vez se presenta con mayor frecuencia en los menores de 65 años[26]. Se define como *"una enfermedad caracterizada por limitación al flujo de aire usualmente progresiva y no completamente reversible que ocurre como consecuencia de un proceso inflamatorio anormal a la exposición de partículas inhaladas; el factor de riesgo más frecuente es la inhalación del humo del tabaco, aunque también se incluyen la de partículas o gases nocivos de origen ocupacional. La enfermedad tiene efectos sistémicos importantes, los cuales pueden responder al tratamiento"*[27-29].

Aún cuando se sabe que existe un elevado nivel de infra-diagnóstico, su prevalencia es variable siendo tres a cuatro veces más frecuente en fumadores que en no fumadores[30]. A nivel mundial, la prevalencia de EPOC en adultos oscila entre el 8,5% y el 11,8% para mujeres y hombres respectivamente[31]. Mientras en Latinoamérica, las diferencias oscilan entre 7.8% en Ciudad de México (México), 19.7% en Montevideo (Uruguay)[32], y 8,9% en Colombia[33], en España se sitúa en el 9,1%[34].

Según los datos de la OMS correspondientes al 2001, la EPOC ocupó la quinta causa de muerte en países desarrollados (3,8% del total) y las proyecciones indican que para el 2020 pasará a ser la tercera causa[17]. Cabe señalar que, a diferencia de otras enfermedades crónicas, la EPOC presenta un perfil de mortalidad creciente[35](figura 7). En el 2001, la EPOC ocupaba el décimo segundo puesto por AVISAs y se prevé que para el 2020 ocupe el quinto puesto[36] correspondiendo al 2% de la carga de todas las enfermedades[37].

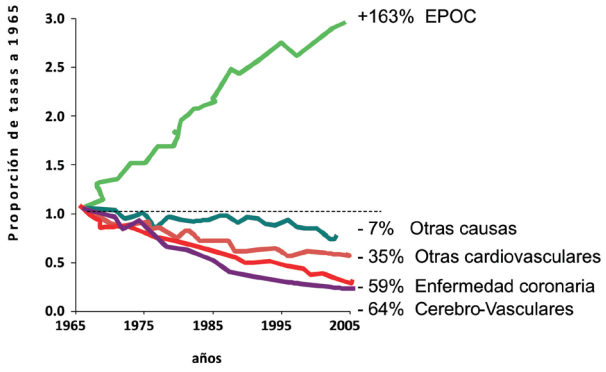

Figura 7: Mortalidad ajustada por edad en EUA por distintas causas entre 1995 y el 2005; la mortalidad por EPOC se incrementó un 163%, mientras que por enfermedad coronaria, otras enfermedades cardiovasculares y cerebro-vasculares disminuyó significativamente, un 59%, 35% y 64% respectivamente[35].

Costes

La EPOC genera un alto coste económico para la sociedad. Los mayores determinantes de los costes directos asociados con la provisión de servicios sanitarios y medicamentos son: las hospitalizaciones por exacerbación y la oxigenoterapia crónica[38]. La magnitud de los costes está directamente relacionada con la gravedad de la EPOC[39]. Desde la perspectiva del pagador, los costes pueden llegar a multiplicarse por 8 o 10 veces en la EPOC grave y muy grave[22;40;41]. Bajo esta misma línea, en Estados Unidos (año 1987) se estimó que el 74% de los costes fueron utilizados por el 20% de los pacientes más severos. Estos costes directos se relacionaron en un 68% con hospitalizaciones por exacerbación o co-morbilidades asociadas[42]. En Europa, en el año 2003, los costes totales sanitarios y no sanitarios de la EPOC alcanzaron los 38.7 billones de € (unos 51.2 billones de US$) y un 60% de ellos se atribuyen a costes indirectos por pérdidas de unos 28.5 millones de días laborales[43]. En la medida en que las exacerbaciones son responsables de un alto porcentaje de hospitalizaciones, puede atribuirse que ellas son responsables de un 40 a 57% de los costes totales[44].

Condiciones patológicas asociadas

Las co-morbilidades han sido clásicamente definidas como aquellas condiciones cínicas que están relacionadas fisiopatológicamente con la enfermedad de base o representan una complicación de la misma; sin embargo, también deben ser consideradas aquellas enfermedades crónicas concurrentes con la enfermedad índice sin relación causal y algunas enfermedades agudas intercurrentes, que se limitan en el tiempo[45;46]. Bajo este amplio espectro, las co-morbilidades acompañan a más del 50% de los pacientes con enfermedades crónicas[47;48], pueden deteriorar su curso clínico y enmascarar su gravedad[49;50]. Su presencia se asocia con un mayor nivel de discapacidad funcional que suele generar dependencia, fragilidad y mal pronóstico[49-51].

En los pacientes con EPOC las co-morbilidades están directamente relacionadas con un mayor deterioro en la calidad de vida, un mayor riesgo de hospitalización y un elevada mortalidad[52;53]. Un 40% de los reingresos hospitalarios fueron causados por co-morbilidad[54], y uno de cada tres pacientes con EPOC tienen entre dos a tres co-morbilidades asociadas[55;56], siendo las cardiovasculares las más frecuentes, seguida por la diabetes mellitus y el cáncer[53;57;58]. Se ha planteado que el síndrome metabólico en los pacientes con EPOC pudiera relacionarse con factores de riesgo comunes a ambas enfermedades (tabaco, sedentarismo, etc.), por lo que se ha sugerido el término de “síndrome inflamatorio sistémico crónico” para describir este fenómeno y explicar, en parte, el origen de los efectos sistémicos de la EPOC y de algunas de las co-morbilidades más frecuentes[59].

Exacerbaciones

Las exacerbaciones de la EPOC se han descrito como episodios intermitentes de agudización de la enfermedad y se han definido como *"un empeoramiento sostenido de la condición basal y estable del paciente, mayor que la variabilidad del día a día y de inicio agudo, que puede justificar un cambio en la medicación regular del paciente con EPOC"* [60]. Su presencia acelera la pérdida progresiva de la función pulmonar y al mismo tiempo ésa pérdida funcional se asocia con una mayor frecuencia de exacerbaciones[61;62]. Se relacionan con deterioro en la calidad de vida[63], mayor riesgo de hospitalización[64;65], y de muerte[66-68].

Se presentan con más frecuencia durante los períodos invernales dada su estrecha relación con los episodios virales de las vías aéreas superiores[69], por lo que son responsables del aumento en la utilización de recursos asistenciales durante este período del año[70]. Aun cuando en un 50% de los casos, las exacerbaciones no son informadas, su frecuencia varía entre 2.5 a 3 exacerbaciones por año[63], y en un 18% requieren hospitalización[40;63].

La mortalidad hospitalaria varía entre el 4 y el 30%, en función de la gravedad del cuadro clínico y la necesidad de vigilancia intensiva. En pacientes ingresados en salas de hospitalización convencional, sin insuficiencia respiratoria grave, la mortalidad intrahospitalaria oscila entre el 5 y el 14%[66], mientras que si el paciente ingresa en una unidad de vigilancia intensiva, la mortalidad puede llegar al 26%[71-73]. La demora en reconocer tempranamente una exacerbación se asocia con tiempos de recuperación más prolongados y un mayor riesgo de hospitalización[74], mientras el fracaso del tratamiento ambulatorio es frecuente y puede alcanzar el 25% de los casos[75;76].

La gestión y el tratamiento de las exacerbaciones de la EPOC

Un mayor conocimiento de los factores de riesgo modificables de las exacerbaciones de la EPOC han sugerido que algunas intervenciones específicas permiten prevenir su aparición[77]: dejar de fumar[78], una adecuada prescripción de la oxigenoterapia crónica domiciliaria[79], programas de rehabilitación pulmonar[80;81], incremento de la actividad física regular[82] y la vacunación contra virus de influenza[83].

Desde hace varios años, la atención centrada en el paciente, con un peso creciente de la atención domiciliaria, ha permitido cambiar radicalmente el concepto del cuidado de los pacientes crónicos. Estrategias de este tipo para prevenir hospitalizaciones, mejorar la calidad de vida y evitar reingresos, han sido exitosas en pacientes con insuficiencia cardíaca congestiva[84-86] y diabetes mellitus[87-89].

En la EPOC, los primeros estudios controlados que analizaron el papel de intervenciones centradas en el domicilio para poblaciones seleccionadas, como la hospitalización domiciliaria[90;91] y el alta temprana[92;93], demostraron ser seguras y coste/eficaces, pero no claramente mejores que la hospitalización convencional. En la misma línea, exis-

ten pocos estudios enfocados a prevenir hospitalizaciones a partir de intervenciones estandarizadas[94;95], por lo que la eficacia de intervenciones de estas características aún no ha sido demostrada de forma fehaciente.

Es decir, tanto para la gestión como para la prevención de las hospitalizaciones por exacerbación de EPOC, es evidente que las intervenciones propuestas en los estudios descritos, no han logrado demostrar los resultados esperados. Por esta razón, se ha postulado que los posibles factores que no han sido tenidos en cuenta de una forma integrada en las diversas intervenciones descritas y que podrían modular este tipo de desenlaces no exitosos en pacientes con EPOC, serían[96;97]:

a) La calificación deficiente de la gravedad de la enfermedad y la presencia de comorblidades no controladas, que los define como pacientes "frágiles".

b) Un soporte social pobre o ausente para el paciente y su entorno, asociados a un frecuente desconocimiento de la enfermedad y de las destrezas necesarias para alcanzar un mejor auto control de la misma.

c) Una integración débil de los profesionales distribuidos entre los distintos niveles de atención del sistema sanitario, encargados de enfrentar la gestión diagnóstica y terapéutica de las enfermedades crónicas.

Sistemas sanitarios y la atención integrada de las enfermedades crónicas

Los sistemas sanitarios vigentes fueron diseñados a mediados del siglo XX y después de más de cincuenta años siguen demostrando un elevado nivel de eficacia para la gestión de enfermedades agudas. Sin embargo, el nivel de fragmentación entre los niveles asistenciales y con los servicios comunitarios, y la atención centrada exclusivamente sobre enfermedades específicas no han permitido afrontar un tratamiento holístico y estructurado para los pacientes con enfermedades crónicas[98]. Esta realidad ha generado múltiples planteamientos alrededor de las políticas futuras para el rediseño de los sistemas sanitarios, que deben afrontar el abismo existente entre lo que el sistema ofrece y lo que debería ofrecer para el cuidado de los pacientes crónicos[99]. El enorme cambio resultante del aumento de la prevalencia de las enfermedades crónicas ha planteado la necesidad de un nuevo paradigma de atención sanitaria para estos pacientes y, con ello, la necesidad de cambios profundos en los sistemas sanitarios[100]. En el 2002, la OMS elaboró el documento "Atención innovadora para las condiciones crónicas: Elementos Fundamentales para la Acción"[14], con el fin de guiar los lineamientos necesarios para la adopción de políticas tendientes a reducir la amenaza que representan las enfermedades crónicas para la población en general, los sistemas sanitarios y sus economías. Este documento basó su estrategia en el concepto de la atención integrada, definida como "la acción coordinada de los sistemas sanitarios para ofrecer, entregar, gestionar y organizar los ser-

vicios relacionados con el diagnóstico, tratamiento, cuidado, rehabilitación y promoción de la salud"[101]. En detalle, esta iniciativa sugiere que un sistema sanitario ideal debería ofrecer: a) una atención continua que se adapte a las necesidades del paciente, b) acceso del paciente a su información para compartir la toma de decisiones sobre su tratamiento, c) compartir información entre los niveles asistenciales, d) basar sus decisiones clínica en la evidencia, e) ofrecer seguridad y transparencia al paciente y su familia, f) anticipar las necesidades del paciente, g) aprovechar los recursos existentes y ahorrar tiempo a los pacientes y h) fomentar la cooperación estrecha entre los profesionales de diferentes niveles asistenciales[99].

De la misma forma, deben replantearse los curricula académicos para que los profesionales sanitarios adquieran las competencias necesarias para trabajar en equipo y potenciar las habilidades necesarias para la atención de los pacientes crónicos[102;103;104;105]. Un elemento esencial de este nuevo paradigma es la preparación de los pacientes y cuidadores para adoptar un rol activo en la gestión de las enfermedades crónicas y la adopción de estilos de vida saludables, a través de su articulación con los servicios comunitarios de soporte social[106;107].

En contexto, la necesidad de diseñar estructuras sanitarias más integrales, que ofrezcan respuestas oportunas a las complejas necesidades de los pacientes crónicos y permitan modular el curso de la enfermedad minimizando el impacto sobre el sistema sanitario, es perentoria.

El modelo de atención integrada

La propuesta que cohesiona los planteamientos descritos anteriormente es el Modelo de Cuidados Crónicos (MCC) formulada por E. Wagner y cols. [108] y posteriormente adoptada por la OMS[14].

El MCC es una concepción funcional de atención integrada a la salud, basado en evidencia científica, centrado en el paciente y coordinado desde el nivel primario de atención, que identifica los elementos esenciales de un cuidado de alta calidad para los pacientes con enfermedades crónicas[97](figura 9). Estos elementos son:

a. El Sistema Sanitario: el sistema debe crear una cultura organizativa que proporcione los mecanismos para promover un cuidado seguro y de alta calidad. Se estimula la interacción y el cuidado compartido de los pacientes entre los equipos multidisciplinarios de atención de la primaria o entre ellos y los especialistas de primaria y el hospital, a través de políticas de mejoramiento continuo e incentivos centrados en la calidad.

b. El auto-control de la enfermedad: empoderar, educar y preparar a los pacientes para asumir el control de su propio cuidado deben ser objetivos centrales del modelo. Estas estrategias de autocontrol para cambiar comportamientos, deben fijar metas puntuales y construir planes de acción individualizados que le permitan al paciente resolver problemas y hacerle un seguimiento oportuno y efectivo. La participación activa del paciente en la toma de decisiones sobre la gestión de su enfermedad, lo estimula a tener una mayor responsabilidad en su cuidado y a entender mejor su pronóstico.

c. El diseño del sistema y su organización: los sistemas deberán ser más proactivos para asegurar un cuidado clínico óptimo y soportar el auto-control de la enfermedad. Deberán definir roles y distribuir tareas entre los miembros del equipo, diseñar estrategias que permitan generar servicios personalizados para la gestión de pacientes complejos y asegurar un seguimiento al trabajo del equipo. En todos los casos el sistema debe modular la intensidad de la atención de acuerdo con el entorno social y cultural del paciente.

d. Decisiones basadas en evidencia: el sistema debe promover un cuidado basado en evidencia y acorde con las necesidades de los pacientes, incorporando las guías de práctica clínica para la toma diaria y regular de decisiones. El uso compartido de las mismas entre los profesionales del equipo y los pacientes, puede estimular la participación de los últimos. El modelo debe ofrecer intervenciones educativas que ayuden a los profesionales a actualizarse regularmente, y que apoyen una atención más segura y de óptima calidad. La incorporación de los especialistas en el nivel primario de atención para que apoyen a los profesionales en casos complejos que generen dudas, debe ser una modalidad efectiva.

e. El sistema de información clínica: la estructura montada debe organizar y facilitar el acceso a los datos de los pacientes a través de la historia clínica y la de los grupos poblacionales por medio de bases de datos relacionales. A esta información podrá accederse rápidamente, para identificar sub-poblaciones de pacientes mas graves que necesiten cuidados mas proactivos, diseñar planes de trabajo compartidos entre los distintos niveles asistenciales, los pacientes y los proveedores y por último seguir el rendimiento del equipo y del modelo de atención propuesto.

f. La Comunidad: se refiere a la movilización de recursos de la comunidad a partir de programas de apoyo social, que apoyen las necesidades de los pacientes que no pueden ser cubiertas por los sistemas sanitarios. Una relación efectiva pero complementaria entre la comunidad y el sistema sanitario debe evitar duplicidades en la atención.

Figura 9: Elementos esenciales del MCC [109]

En la era de internet, los pacientes se cuestionan para bien o para mal las propuestas que se plantean alrededor de su enfermedad[110]. Un aspecto muy relevante para la implementación de este tipo de sistemas, está en el interés progresivo por parte de los pacientes para participar en la toma de decisiones sobre el manejo de su propia enfermedad y sobre las implicaciones pronosticas de estas decisiones. Ello rompe con el esquema clásico y paternalista de la relación profesional-paciente, donde el primero tomaba siempre las decisiones por el segundo[111]. Estos procedimientos denominados como toma de decisiones compartidas, apoyan los procesos de auto-control dentro del modelo[112].

La atención integrada en la EPOC

La experiencia para la implementación de este tipo de intervenciones ha sido muy exitosa en otras enfermedades distintas a la EPOC, como la diabetes[113], la insuficiencia cardíaca congestiva[114-116] y el asma[117]. Las características de la EPOC abren expectativas especialmente positivas para la aplicación de estrategias de atención integrada en los diferentes niveles de prevención (primaria, secundaria y terciaria). En primer lugar, y a pesar de un elevado nivel de infra-diagnóstico de la enfermedad, que en muchos casos se logra durante una primera hospitalización por exacerbación, es bien conocido como la modulación de algunos factores de riesgo modificables, como el tabaquismo, la inactividad física o el síndrome metabólico, pueden incidir, sobre el curso clínico de la EPOC. La articulación entre el tratamiento farmacológico y no farmacológico y el tratamiento óptimo de las comorbilidades son objetivos prioritarios. Finalmente, las complejidades inherentes en las fases avanzadas de la EPOC y la frecuente aparición de recaídas como exacerbaciones de la enfermedad, también podrían afrontarse con mayor éxito con los nuevos planteamientos de carácter integrado[118-120].

En segundo lugar, es evidente que una característica innovadora para este tipo de pacientes, ha sido el desarrollo de propuestas de prestación de servicios en el domicilio del

paciente con el soporte de tecnologías amigables, cuyo papel fundamental sería apoyar un mejor control a distancia en cualquiera de los niveles de atención, con especial énfasis en las interacciones con y entre los proveedores de los servicios[121]. Bajo esta concepción, es cada vez es más evidente la importancia de involucrar las tecnologías de la información y la comunicación (TIC) como elemento fundamental para trasformar la estructura de los sistemas sanitarios[122]. Una plataforma tecnológica que permita compartir información entre profesionales y de estos con el paciente, es un elemento de soporte importante para los servicios de atención integrada[123]. La hipótesis de partida es que la utilización adecuada de las TIC mejorará la calidad de la atención integrada de las enfermedades crónicas [14;124-126].

Bajo esta perspectiva nació el proyecto CHRONIC[127], concebido para desarrollar estrategias en el domicilio del paciente que permitieran evaluar el papel de intervenciones basadas en el MCC y soportadas por soluciones tecnológicas basadas en internet. Para lograr el objetivo, el proyecto se cimentó en el desarrollo de protocolos clínicos de atención domiciliaria para pacientes con EPOC.

La presente tesis doctoral pretendió validar intervenciones de atención integrada orientadas para la gestión de las exacerbaciones graves de los pacientes con EPOC. Para lograr estos objetivos, el grupo de trabajo planificó el desarrollo no simultáneo de dos estudios clínicos controlados que permitieran responder los interrogantes propuestos. Ambos fueron diseñados para buscar el impacto de nuestras intervenciones para prevenir y/o modular las exacerbaciones de la EPOC. El primer estudio, al que denominamos de forma genérica como HOSPITALIZACION DOMICILIARIA, de seguimiento corto y con un talante más centrado en la gestión aguda de episodios de exacerbación en el domicilio del paciente para evitar recaídas, produjo los manuscritos 1, 2 y 3 de esta tesis. El segundo estudio, al que denominamos como PREVENCION DE HOSPITALIZACIONES, de enfoque más preventivo y orientado a evitar hospitalizaciones no planeadas por exacerbación durante un año de seguimiento, produjo los manuscritos 4 y 5 de esta tesis. Como material adicional, que apoye la discusión de los resultados obtenidos se anexa al final de la tesis, la editorial que mereció el manuscrito 4.

HIPOTESIS Y OBJETIVOS

HIPOTESIS PRINCIPAL

Un modelo de atención integrada flexible, de carácter distributivo, centrado en el paciente y enfocado hacia la gestión domiciliaria de los episodios graves de exacerbación y la prevención de hospitalizaciones por exacerbación de la EPOC, es eficaz y contribuye a la contención de costes. Su desarrollo se basará en el diseño y validación de intervenciones asistenciales estandarizadas dirigidas a grupos específicos de pacientes con objetivos clínicos bien definidos.

OBJETIVOS GENERALES

1. Diseñar y validar una intervención de hospitalización domiciliaria y alta precoz basada en la atención integrada de los pacientes con exacerbación de EPOC. La intervención se orienta al tratamiento domiciliario de pacientes con episodios graves que hubieran requerido ingreso hospitalario en un esquema clásico de atención convencional.

2. Diseñar y validar una intervención basada en atención integrada destinada a la prevención de hospitalizaciones no planeadas por exacerbación de la EPOC en pacientes con historia de una o más hospitalizaciones previas por causa semejante.

OBJETIVOS ESPECIFICOS

ESTUDIO HOSPITALIZACION DOMICILIARIA

Manuscrito 1

Home hospitalisation of exacerbated chronic obstructive pulmonary disease patients Eur Respir J 2003; 21: 58–67

Evaluar la eficacia de un programa de hospitalización domiciliaria para tratar los episodios de exacerbación de la EPOC; los resultados esperados serán una reducción en las recaídas

que motiven nuevas visitas en el servicio de urgencias, un mejor autocontrol de la enfermedad y una mejor calidad de vida.

Manuscrito 2

The impact of home hospitalization on healthcare costs of exacerbations in COPD patients
Eur J Health Econ. 2007; 8 (4):325-32

Evaluar el impacto de los factores determinantes de la reducción de costes asociados a la exacerbación de la EPOC y el potencial de contención de costes generado por el programa de hospitalización domiciliaria.

Manuscrito 3

Early Relapses After Severe Exacerbations in Patients with Chronic Obstructive Pulmonary Disease (Submitted)

Identificar los factores de riesgo asociados con un mayor número de reingresos hospitalarios o muerte durante las 8 semanas posteriores a un episodio de exacerbación de la EPOC, en el marco de un programa de hospitalización domiciliaria.

ESTUDIO PREVENCION DE HOSPITALIZACIONES

Manuscrito 4

Integrated care prevents hospitalisations for exacerbations in COPD patients
Eur Respir J 2006; 28: 123–130

Evaluar la eficacia de un modelo de atención integrada a nivel de atención primaria y hospitalaria apoyado en una plataforma tecnológica, para prevenir hospitalizaciones no planeadas por episodios de exacerbación de la EPOC en pacientes con antecedentes de hospitalizaciones previas.

Manuscrito 5

Effects of an integrated care intervention on risk factors of COPD readmission
Resp Med 2007; 101: 1462–1469

Evaluar la eficacia de la atención integrada para generar cambios positivos en la calidad de vida, el estilo de vida y el auto-control de la enfermedad de durante un programa de prevención de hospitalizaciones por exacerbación de EPOC, e identificar si aquellos cambios que pueden explicar la reducción en las hospitalizaciones.

TRABAJOS ORIGINALES

Manuscrito 1

Home hospitalisation of exacerbated chronic obstructive pulmonary disease patients

Eur Respir J 2003; 21: 58–67

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Home hospitalisation of exacerbated chronic obstructive pulmonary disease patients

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ABSTRACT: It was postulated that home hospitalisation (HH) of selected chronic obstructive pulmonary disease (COPD) exacerbations admitted at the emergency room (ER) could facilitate a better outcome than conventional hospitalisation.

To this end, 222 COPD patients (3.2% female; 71±10 yrs (mean±SD)) were randomly assigned to HH (n=121) or conventional care (n=101). During HH, integrated care was delivered by a specialised nurse with the patient's free-phone access to the nurse ensured for an 8-week follow-up period.

Mortality (HH: 4.1%; controls: 6.9%) and hospital readmissions (HH: 0.24±0.57; controls: 0.38±0.70) were similar in both groups. However, at the end of the follow-up period, HH patients showed: 1) a lower rate of ER visits (0.13±0.43 *versus* 0.31±0.62); and 2) a noticeable improvement of quality of life (Δ St George's Respiratory Questionnaire (SGRQ), -6.9 *versus* -2.4). Furthermore, a higher percentage of patients had a better knowledge of the disease (58% *versus* 27%), a better self-management of their condition (81% *versus* 48%), and the patient's satisfaction was greater. The average overall direct cost per HH patient was 62% of the costs of conventional care, essentially due to fewer days of inpatient hospitalisation (1.7±2.3 *versus* 4.2±4.1 days).

A comprehensive home care intervention in selected chronic obstructive pulmonary disease exacerbations appears as cost effective. The home hospitalisation intervention generates better outcomes at lower costs than conventional care.

Eur Respir J 2003; 21: 58–67.

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Chronic respiratory diseases are an important burden on healthcare systems worldwide [1] that is expected to increase over the forthcoming 2 decades [2], particularly due to chronic obstructive pulmonary disease (COPD). Winter outbreaks of COPD exacerbations mostly occurring in elderly people with concurrent chronic comorbidities often generate dramatic increases in hospital emergency room admissions with subsequent dysfunctions in the healthcare system. It is estimated that hospitalisations of COPD exacerbations represent ~70% of the overall costs associated with the management of the disease [3].

A first feasibility analysis of home-based services to prevent conventional hospitalisations of COPD exacerbations was reported in 1999 by GRAVIL *et al.* [4]. Three subsequent controlled trials [5–7] also conducted in the UK have demonstrated both safety and cost reduction when these types of services were applied to selected COPD patients. It is worth noting, however, that none of these studies or the most recent report by SALA *et al.* [8] showed higher efficacy than conventional hospitalisation in terms of prevention of short-term relapses.

The present investigation was conducted on COPD exacerbations admitted at the emergency room of two tertiary hospitals in the Barcelona area. It was postulated that home hospitalisation with free patient phone access to a specialised nurse should generate a better outcome at lower direct costs than inpatient hospitalisation. Namely: 1) a lower rate of emergency room (ER) relapses; 2) a greater improvement of health-related quality of life (HRQL); and 3) better patient self-management of the disease.

The clinical trial was performed as a preliminary

step prior to the setting of a technological platform that includes a web-based call centre as one of the core elements [9].

Methods

Study groups

Over a 1-yr period (1st November 1999 to 1st November 2000), 222 patients with COPD exacerbations were included in the study among those admitted at the ER of two tertiary hospitals, Hospital Clínic and Hospital de Bellvitge of Barcelona, Spain. The two primary criteria for inclusion in the study were COPD exacerbation as a major cause of referral to the ER [10] and absence of any criteria for imperative hospitalisation as stated by the British Thoracic Society (BTS) guidelines [11] (*i.e.*, acute chest radiograph changes, acute confusion, impaired level of consciousness, and arterial pH <7.35). All COPD exacerbations admitted at the ER on weekdays (Monday to Friday, from 09:00 am to 04:00 pm) during the study period (n=629) were screened by a specialised respiratory team (one chest physician and one nurse) in each hospital. As displayed in the study profile (fig. 1), 220 patients (35%) showing one of the following exclusion criteria were not considered candidates for the programme: 1) not living in the healthcare area or admitted from a nursing home (11.5%, n=72); 2) lung cancer and other advanced neoplasms (5.9%, n=37); 3) extremely poor social conditions (5.2%, n=33); 4) severe neurological or cardiac comorbidities (4.8%, n=30); 5) illiteracy (4.8%, n=30); and 6) no phone at home (2.8%, n=18). One-hundred and sixty-five (26.2%) of the 629 screened patients required imperative hospitalisation. Up to 244 patients (38.8%) were considered eligible for the study, but 22 subjects (3.5%) did not sign the informed consent after full explanation of the characteristics of the protocol. The remaining 222 patients (35.3%) were blindly assigned using a set of computer-generated random numbers in a 1:1 ratio either to the treatment group (home-based hospitalisation (HH)) or to the control group (conventional care). One of the hospitals (Hospital Clínic) used a 2:1 randomisation ratio during the first 3 months of the study, which explains the difference in number between the two groups (HH: 121 patients; conventional care: 101 patients).

Home hospitalisation intervention

Only patients assigned to HH were assessed by a specialised team. The characteristics of the intervention are summarised in the Appendix. The HH intervention had three main objectives: 1) an immediate or early discharge from the hospital was encouraged by the specialised team aiming to either avoid or reduce the length of inpatient hospitalisation; 2) a

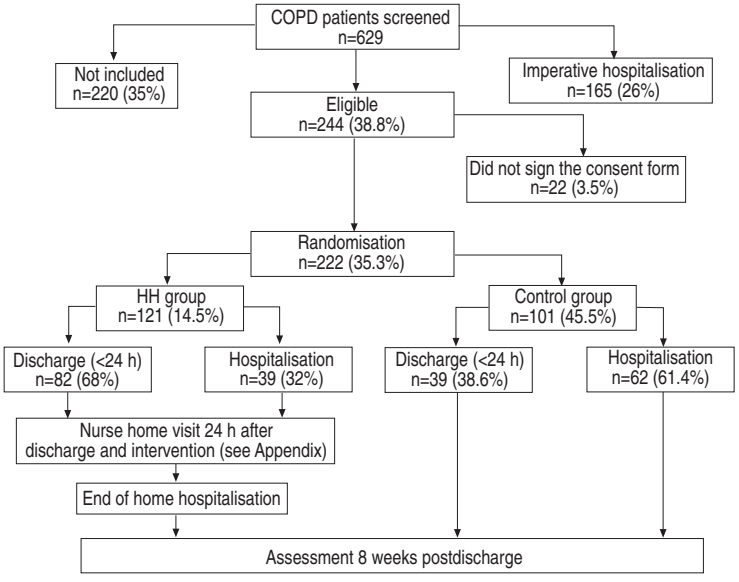

Fig. 1. – Study profile. From the 629 patients screened, 26% (n=165) required imperative hospitalisation [11] while up to 35% (n=220) were not eligible (see text). The remaining 244 patients (38.8%) were candidates for the study, but 22 patients (3.5%) did not sign the consent form. Two-hundred and twenty-two patients were included (home hospitalisation: 121 and conventional care: 101). COPD: chronic obstructive pulmonary disease; HH: home hospitalisation.

comprehensive therapeutic approach was tailored on an individual basis, according to the needs detected by the specialised team; and 3) patient support by a skilled respiratory nurse either through home visits or free-phone consultation was ensured during the 8-week follow-up period. For each HH patient, a first home visit was scheduled by the nurse within 24 h after discharge. The length of the home hospitalisation was set by the respiratory nurse. A maximum of five nurse visits at home were permitted during the 8-week follow-up period, but patient′s phone calls to the nurse were not limited in number. The intervention was considered to be a failure if one of the two following events occurred: the patient relapsed and required referral to the ER; or >5 nurse visits at home were needed during the follow-up period. In both circumstances, the patients were analysed in the study but they were not considered for a new randomisation (*i.e.* when attended at the ER for the relapse).

Standard pharmacological treatment was used following COPD guidelines of the Spanish Respiratory Society (SEPAR) [10] during HH and conventional care. Nonpharmacological interventions for HH patients, summarised in the Appendix, were performed following specific guidelines [12]. Fragility factors that might facilitate COPD exacerbations were arbitrarily defined by consensus of the research team pre-hoc: 1) severity of pulmonary disease (hypercapnia, cor pulmonale); 2) active comorbidities; 3) poor knowledge of the disease; 4) poor compliance with treatment; 5) inadequate skills for the administration of inhaled therapy; 6) low level of social support; and 7) anxiety and/or depression. All of these factors were evaluated both at the initial assessment and then at completion of the follow-up using standard questionnaires, as described below. The response to therapy at home was evaluated by the nurse, based on clinical judgment plus measurements of vital signs and pulse oximetry (Monitor Pulsox^{TM}-^{3i}; Minolta, AVL Medical Instruments AG, Osaka, Japan). Arterial blood sampling at home for respiratory gases was performed if needed. The nurse′s phone access to the physician at the hospital for remote supervision was ensured. Assessment of the progress of the active patients as well as decisions on potential changes in treatment prescription was done during weekly meetings of the specialised team.

Conventional care group

Patients included in the conventional care group (controls) were evaluated by the attending physician at the ER who decided either on inpatient hospital admission or discharge. Pharmacological prescriptions followed the standard protocols of the centres involved in the study which were similar in the two groups (HH and controls) [10], but the support of a specialised nurse at the ER and at home was not provided for controls. At discharge, the patient was usually supervised by the primary care physician who was not aware of the protocol.

Initial assessment and evaluation 8 weeks after discharge

Initial assessment at admission to the study was identical for both groups patients and included evaluation of the BTS [11] criteria of severity of the exacerbation and blind administration of a questionnaire, described in detail elsewhere [13], about: 1) risk factors for exacerbation (vaccination, smoking habits, comorbidities); 2) HRQL status during the previous year (St George′s Respiratory Questionnaire (SGRQ) [14] and Short-Form 12-item survey (SF-12) [15]); 3) history of previous exacerbations (1 yr) requiring inpatient hospitalisations and/or ER admissions evaluated, at least, by questionnaire and, at the most, also by examination of individual clinical records; 4) clinical features of the current exacerbation; 5) fragility factors; and 6) treatment, including compliance, observed skills for administration of inhaled drugs, and rehabilitation at home. Home rehabilitation included interventions, such as manoeuvres to facilitate sputum clearance, nutrition recommendations and skeletal muscle exercise of both upper and lower limbs. Vital signs, chest radiograph films and arterial blood gases were obtained in all patients on admission.

After the 8-week follow-up period, the same questionnaires were administered again to the two groups. In addition, a detailed list of questions on the utilisation of healthcare resources during this period was included. Forced spirometry, chest radiograph films and arterial blood gases were also obtained. A questionnaire to evaluate patient′s satisfaction was also blindly administered.

Healthcare costs

Costs were calculated for each group from the perspective of the public insurer, such that, the cost analysis was restricted to direct healthcare costs. Other resources implied in the programme, such as patient labour time and informal care, were not evaluated in this study.

First, the relevant categories to be considered in order to estimate cost at patient level were identified: 1) length of hospital stay (days of initial hospitalisation plus days during hospital readmissions); 2) ER visits not requiring admission to the hospital; 3) hospital outpatient visits to specialists; 4) primary care physician visits; 5) visits for social support; 6) nurse visits at home; 7) treatment prescriptions; 8) phone calls; and 9) transportation services. Data on use of categories were obtained for each patient during the follow-up period.

A second step was the valuation of resource use. The total cost for each category was calculated as the product of the number of events multiplied by the unit cost per event (*i.e.* hospitalisation costs were calculated as days in hospital including initial stay plus readmissions multiplied by the average hospitalisation cost per day). Unit costs are expressed as year 2000 prices using Euros (€) as the monetary unit in the European Union. Costs for nurse visits at home, drug

prescriptions, phone calls and transportation services were directly calculated using information about labour cost, market prices, including value added tax, and overhead costs. Hospital unit costs per hospital stay and visits were not available in the hospitals participating in the study. Instead, average specifically observed tariffs for COPD patients in a public insurance company covering the civil servants of the City Council of Barcelona (PAMEM) were used. These tariffs are mainly paid to public and nonprofit hospitals, and have a close relationship with the real costs. In fact, tariffs represent an adequate basis for cost estimates, given that the present authors' interest is in the financial costs for third party insurers [16].

Statistical analysis

Results are expressed as mean±SD or as percentages in the corresponding categories. Comparisons between the two study groups on admission and 8 weeks after discharge and changes during the follow-up period were performed using independent t-tests, a nonparametric test (Mann-Whitney U-test) or the Chi-squared test. Changes within each group were assessed using t-test or nonparametric Wilcoxon test for paired samples. Statistical significance was accepted at $p<0.05$.

Results

Assessment on first emergency room admission

Patients of the HH group and controls showed similar characteristics on ER admission (table 1). HRQL was also similar (SGRQ total score, 58±17 *versus* 59±20, HH and conventional care, respectively; SF-12 physical, 36±8 *versus* 34±8; and, SF-12 mental, 44±12 *versus* 44±13, respectively). No differences between groups were observed in knowledge of the disease and in self-management of the chronic condition (fig. 2). On average, the two groups showed a relatively acceptable compliance to oral therapy (79% of the patients), inhaled therapy (66%), and long-term oxygen therapy (82%). However, they showed poor results in knowledge of the disease (only 20% of the patients were fully aware of their disorder), appropriate inhalation technique (26%), and rehabilitation therapy at home (10%). Forced spirometric measurements at week 8 after discharge did not show differences between the two groups (table 1).

Outcomes

Five patients (4.1%) in the HH group and 7 controls (6.9%) died during the 8-week follow-up period (table 2). The rate of hospital readmissions during this period was ~25%, with no differences between

Table 1. – Baseline characteristics of the study groups

	Home hospitalisation	Conventional Care	Total
Subjects n (% female)	121 (3.3)	101 (3.0)	222 (3.2)
Age yrs	71.0±9.9	70.5±9.4	70.8±9.7
Respiratory rate·min^{-1}	26.9±6.0	26.8±5.9	26.8±5.9
Dyspnoea score (VAS)	6.1±3.1	6.2±3.3	6.2±3.2
Risk factors			
Influenza vaccination %	66.1	65.3	65.8
Current smokers %	27.3	17.8	23.0
Comorbidities %	93.4	96.0	94.6
Number of comorbid conditions	2.9±1.8	3.1±1.6	3.1±1.7
Exacerbations requiring in-hospital admission (previous year)			
Subjects %	40.8	40.6	40.7
Number of episodes	0.7±1.2	0.9±1.4	0.8±1.2
Oxygen therapy at home			
Patients %	12.4	18.8	15.3
Arterial blood gases (on admission)			
F_{I,O_2}	21.7±1.4	22.1±2.3	21.9±1.8
pH	7.4±0.04	7.4±0.3	7.4±0.2
P_{a,O_2}	65.0±13.6	64.7±16.4	64.9±14.9
P_{a,CO_2}	42.7±7.5	43.8±8.9	43.2±8.2
Blood sampling at F_{I,O_2}=0.21 % patients	77.6	72.6	75.4
P_{a,O_2} breathing F_{I,O_2}=0.21	63.2±10.5	62.9±13.9	63.1±12.1
Forced spirometry (at 8 weeks of follow-up)			
FVC L (% pred)	2.4±0.9 (64)	2.2±0.9 (60)	2.3±0.9 (62)
FEV_1 L (% pred)	1.2±0.6 (43)	1.1±0.4 (41)	1.1±0.5 (42)
FEV_1/FVC %	50±13.3	50±13.1	50±13.2

Results are expressed either as mean±SD or as a percentage of subjects in the corresponding category. Total: combined data of the two groups; VAS: visual analogue scale for scoring dyspnoea; F_{I,O_2}: inspiratory oxygen fraction; pH: arterial pH; P_{a,O_2}: oxygen tension in arterial blood; P_{a,CO_2}: carbon dioxide tension in arterial blood; FVC: forced vital capacity; pred: predicted; FEV_1: forced expiratory volume in one second; FEV_1/FVC: ratio, expressed as an actual value.

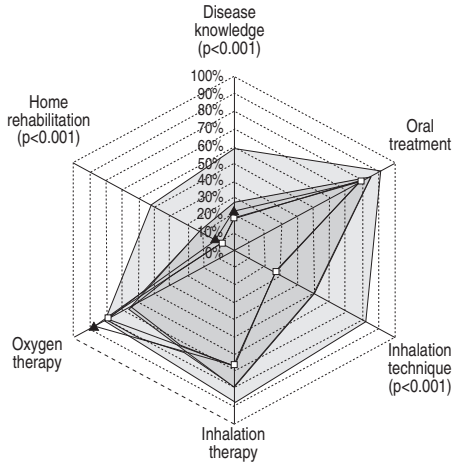

Fig. 2. – Knowledge of the disease and self-management of the chronic condition. Results are expressed as per cent of patients. On admission (inner limits: home hospitalisation (HH): ▲; controls: □), no differences were seen in any of the six dimensions of the graph. No changes in the control group (dark grey area) were seen during the 8-week follow-up period, but marked beneficial effects were detected in the HH group (light grey area).

groups. In the control group, however, the rate of relapses requiring new ER admission without subsequent hospital readmissions almost doubled the figure shown by the HH patients ($p<0.05$). As indicated in table 2, the HH group showed higher improvement in HRQL and higher satisfaction than the control group after the 8-week follow-up period. Furthermore, a higher percentage of patients in the HH group (fig. 2) had a substantial improvement in knowledge of the disease (HH 58% *versus* 27% for controls, $p<0.01$), compliance on inhalation technique (HH 81% *versus* 48% for controls, $p<0.001$), and rehabilitation at home (HH 51% *versus* 21% for controls, $p<0.01$).

Characteristics of inpatient hospitalisation

Up to 68% of HH patients were discharged from ER without requiring hospitalisation (<24 h) compared to 39% of the control patients ($p<0.001$; table 2). Consequently, the length of hospitalisation was also significantly lower in the HH group than in controls (1.7 *versus* 4.2 days, respectively; $p<0.001$). Hospitalisation for >3 days was required in 48% of controls but only 17% of HH patients. Characteristics of inpatient hospitalisation in the two groups are reported in table 2. The average length of the stay in the hospitalised patients of the control group was 8.1 days.

Table 2. – Main outcomes of the study and characteristics of the initial inpatient hospitalisation

	Home hospitalisation	Conventional care	p-value
Clinical outcomes (8-week follow-up)			
Inpatient hospital readmissions			
Patients n (%)	23 (20.0)	26 (27.7)	
Number of episodes	0.24±0.57	0.38±0.70	
Emergency room readmissions			
Patients n (%)	11 (9.6)	21 (22.3)	0.02#
Number of episodes	0.13±0.43	0.31±0.62	0.01¶
Deaths n (%)	5 (4.1)	7 (6.9)	
Health-related quality of life (8-week follow-up)			
Mean ΔSGRQ score			
Total	-6.9	-2.4	0.05+
Symptoms	-8.7	-8.4	
Activity	-4.8	-0.09	
Impact	-7.6	-1.9	0.03+
Mean ΔSF-12 score			
Physical	1.7	1.9	
Mental	2.0	-0.05	
Patient's satisfaction			
Mean score	8.0	7.5	0.03¶
Inpatient hospitalisation			
% of patients hospitalised			
<1 day %	67.8	38.6	<0.001#
2 days %	5.8	4.0	
3 days %	9.9	9.9	
>3 days %	16.5	47.5	
Days of hospitalisation	1.71±2.33 [0–11]	4.15±4.10 [0–16]	<0.001¶

Results are expressed either as mean±SD or as a percentage of subjects in the corresponding category. Minimum and maximum values are expressed in square brackets. SGRQ: St George's Respiratory Questionnaire; SF-12: Short-Form 12-item survey. #: Chi-squared test; ¶: Mann-Whitney U nonparametric test for independent samples; +: t-test for comparison of two independent samples.

In the HH group, the average length of the home-based hospitalisation was 3.56 days (1–14 days). During the 8-week follow-up period, the number of nurse visits at home was 1.66±1.03 (range, 0–4) and the number of nurse phone calls to patients was 1.56±1.31 (0–6). Likewise, the number of patients' phone calls to the nurse was 0.76±1.34 (0–9), such that the overall number of phone calls was 2.33±2.05 (0–10).

As indicated in table 3, the control group showed a higher average cost per patient than the HH group in terms of length of hospitalisation and ER visits. Conversely, the control group displayed lower costs for prescription than HH. During the follow-up period, no differences between the two groups were seen in the use of the following three categories: visits to primary care physician, transportation, and social support. The average overall healthcare cost per patient in the HH group was only 62% of the average cost calculated for control patients (€1,255 *versus* €2,033; p= 0.003).

Discussion

The present study indicates that home hospitalisation as described in the Appendix generated better outcomes than conventional care of COPD exacerbations. Better outcomes with HH included: 1) lower hospitalisation rates; 2) lower rates of short-term relapses requiring ER admissions; 3) clinically relevant improvement in HRQL, as assessed by the SGRQ [17]; 4) a higher degree of patient satisfaction; and 5) an important positive impact on knowledge of the disease and on patient self-management of the chronic condition.

The results were obtained with a rather modest use of the resources allocated to home support. Only a small portion of the five potential nurse visits was used (on average 1.7 nurse visits at home) during the 2-month follow-up period. Despite the free-phone access that was ensured to all patients, the average number of patients' phone calls to the nurse was only 0.76. Somewhat unexpectedly, the study shows that home hospitalisation was less costly than conventional care. The average overall costs per HH patient were substantially lower than in conventional care, essentially due to fewer days of inpatient hospitalisation. Slightly higher costs in the HH group were only observed in prescriptions that were due to both oxygen therapy and nebuliser therapy, because these two treatments were part of the inpatient hospitalisation costs in a substantial portion of the control group.

While all previous studies assessing either home hospitalisation or early discharge [5–8] have essentially shown that the approach is safe, this is the first report that clearly demonstrates the beneficial effects of the intervention compared with conventional care of COPD exacerbations. The present study also indicates that improvement of the outcomes can be associated with a reduction of direct costs. Like other reports [5–8], the present study confirms that home hospitalisation is suitable only in a subset of exacerbations that must be selected at the hospital after proper assessment by a specialised team.

Internal validity of the trial

The validity of the assignment process for either HH or conventional care was ensured by both the generation of the allocation sequence by a random

Table 3. – Average direct cost per patient for the two study groups

Categories	Costs per category €	Home hospitalisation		Conventional care		p-value#
		No. of events/ patients	Cost per patient €	No. of events/ patients	Cost per patient €	
Inpatient hospital stay	220.62	495/77	941.40	765/81	1795.47	<0.001
ER visits	79.71	15/11	10.31	29/21	24.59	0.01
Outpatient visits	39.85	16/12	5.49	52/14	22.04	
Primary care physician visits	47.48	20/6	8.19	15/8	7.57	
Social support visits	18.75	10/3	1.62	11/4	2.19	
Nurse home visit	25.34	192/101	41.94			
Prescriptions			217.21		172.06	0.001
Phone calls:						
Patient to nurse		88/46				
Nurse to patient		182/96				
Total	9.02	270/99	20.99			
Transport	6.01	154/77	7.97	150/61	9.59	
Average direct cost per patient (95% CI)			1255.12 (978.54–1568.04)		2033.51 (1547.05–2556.81)	0.003

Costs are expressed in Euros (€) at year 2000 prices. Cost per category indicates the estimated average unit cost (*i.e.* cost of one day of inpatient hospitalisation). Number of events/patients is the number of units of the corresponding category and number of active patients in that category, respectively. The average cost per patient for a given category normalised by group size was calculated as the product of the unit cost per category (one event) multiplied by the number of events divided by the total number of patients in the group (home hospitalisation, n=116 or conventional care (controls), n=94, dead patients were not taken into account in the calculation). CI: confidence interval. #: Mann-Whitney U nonparametric test.

process and preventing any foreknowledge of the treatment assignments by the specialised team that implemented the allocation sequence [18]. As described in the Methods section, one of the hospitals (Hospital Clínic) transiently used a 2:1 randomisation ratio as a conservative approach to ensure an adequate number of HH patients. This strategy provoked a lack of equilibrium in the number of patients assigned to each group (HH: 121; controls: 101), but does not seem to compromise the comparability between the two groups, as shown by the similar results obtained in the assessment on admission.

Since missing data represented <2% of the study group, it can be considered that the aims of the follow-up analysis were fully achieved. It is worth noting, however, that the relatively short follow-up planned in the study might have reduced the impact of the positive effects shown by educational intervention (fig. 2). The pivotal effects of education on self-management of asthma have been widely demonstrated in recent years [19, 20] and evidence of this has recently been reported for COPD patients [21]. The present study identifies this area as a key field for the development of future guidelines for chronic respiratory diseases.

In the economical analysis, the limitation of self-reported use of healthcare resources was partially palliated by the evaluation of the clinical records of the patients. An excellent correlation between the two scores was observed. The economic evaluation performed in the context of this randomised controlled trial was designed to ask the following question: does substituting hospital-at-home care for hospital care in COPD exacerbations result in a lower cost to the health service?

This economic evaluation may be affected by two main limitations. First, the perspective of the evaluation was that of the public healthcare insurer, excluding nonhealthcare costs. In this study, formal (paid work) or informal (unpaid work and leisure time) care for exacerbated COPD patients were not evaluated. Notwithstanding, a previous randomised controlled trial comparing hospital-at-home care with inpatient care [22] reported that carers' expenses made up a small proportion of total costs and inclusion of these costs did not alter the results.

A second limitation of the economic evaluation is that average costs were used to evaluate hospital care. In fact, hospital resources released for the care of other patients may be less than the final average cost when patients are nearing the end of their hospital stay and therefore require less resource intensity (marginal cost). It has been argued that the existence of fixed hospital costs amplifies the value of any potential savings resulting from a reduction in bed-days [23].

However, marginal costs estimated as the short-run variable costs are not appropriate to evaluate the costs (or savings) that would be associated with the provision of new hospital services in the long-term [24]. From the theoretical point of view, average costs may appropriately represent the value of freed resources, assuming that patients can be admitted to empty beds. Even so, a sensitivity analysis was performed assuming that resources released by home hospitalisation intervention (days of hospital) would be either 75% or 50% of the average cost. Under both assumptions, it was found that the average cost per patient in the HH group was lower than the cost calculated for control patients. It may therefore be asserted that using marginal cost to evaluate resources does not result in home hospitalisation being more costly than conventional care for exacerbated COPD patients.

External validity

The positive outcomes obtained in the study probably reflect the combined effects of the comprehensive home care intervention (Appendix) undertaken in this trial. It is worth noting, however, that while the reduction of ER readmissions in the HH group was clear, the impact on short-term hospital readmissions was rather modest, as seen in other reports [5].

It is remarkable that the results of the present study fully substantiate and amplify the message given by studies [5, 6] carried out in the UK, despite noticeable country differences in terms of interactions between primary care and tertiary hospitals. While in Barcelona, ~70% of the ER admissions in tertiary hospitals for COPD exacerbations corresponded with self-referrals [25]. This figure falls to ~30% on average in the UK and as low as 1% in the report by SKWARSKA *et al.* [5]. The present results seem to support the notion that the efficacy of HH is not dependent on the specificities of the healthcare system if the logistics of the home care services are fully managed by the hospital. Whether this type of setting should be recommended or not is still controversial. Alternatively, a distributed model based on a close collaboration between healthcare levels [26, 27] has been suggested, as discussed below.

Although the current investigation purposely followed general aspects of the study profile reported by SKWARSKA *et al.* [5], a proper comparative analysis between the two studies is difficult because of several factors. First, differences in the healthcare systems are not negligible as alluded to above. Second, the Scottish patients were randomised after ER doctors had already decided on hospital admission, which was not the case in the present study. This factor might have resulted in a selection of more severe patients in the two groups (HH and controls) in [5] as compared to the present study. It can be speculated that the clear beneficial effects described in the present investigation (not seen in [5]) might be because patients in Barcelona had less severe exacerbations. It is worth noting that UK studies [4–7] on different modalities of home hospitalisation consistently showed, on average, lower FEV_1, higher SGRQ scores and lower rates of autoreferrals to ERs of tertiary hospitals than in studies carried out in Spain [8, 13], suggesting that sicker patients were attending in UK hospitals. This is probably due to country differences in the interactions between healthcare levels.

It can be concluded, however, that an assignment bias was not present in these two studies. Moreover, the patients of the present study showed similar characteristics to those reported by studies on

exacerbated COPD patients admitted in the ER of tertiary hospitals in Spain [8, 13].

There is controversy regarding the effects of hospital-at-home schemes on costs for COPD patients. Two randomised controlled trials [22, 23] reported that hospital-at-home significantly increased healthcare costs for COPD patients. The two trials, however, analysed a very small sample of patients whose severity of illness was not delineated.

The economic evaluation of home hospitalisation in the current study clearly reported cost savings. As stated in the Results section, savings may be mainly attributed to the reduction in the length of stay for patients in the HH programme. The magnitude of this reduction in the present study is enough to compensate the increase in the costs corresponding to the HH programme. In this sense, the present results confirm the importance of the impact of the intervention on the use of this resource for COPD patients in the economic evaluation of home care programmes as the sensitivity analysis of SHEPPERD *et al.* [22] indicated.

Implications for healthcare policy

The search for healthcare services meeting the needs of chronically ill people [26, 27] has recently generated the so-called chronic care model [28]. These authors propose a patient-centred approach, with special emphasis on shared care arrangements across the healthcare system (between specialised care at the hospital and primary care) and within the multidisciplinary primary care team. Key features of the model [28] are the development of innovative home-based services with involvement of patients (and caregivers) as partners in the management of the disease.

A key challenge in the development of such new services is a redefinition of the roles and skills of the specialised nurses and physiotherapists [29, 30]. The interactions of these allied healthcare professionals with physicians should be re-examined. Adequate standardisation of procedures is also needed. In this new setting, there is an important role for the use of information technologies, facilitating the interactions between healthcare levels and the development of novel educational tools.

It can be concluded that home hospitalisation of selected chronic obstructive pulmonary disease exacerbations generates better outcomes at lower costs than conventional care. The data of the present study suggests that managerial aspects of exacerbated chronic obstructive pulmonary disease patients must be revisited. Home-based services (home hospitalisation or home support) should be taken as part of the continuum of care in chronically ill patients. Despite the promising results of these new approaches in the treatment of chronic obstructive pulmonary disease exacerbations, prevention of early relapses after discharge is still an important challenge. The present study prompts the need for the deployment of this type of intervention as a regular healthcare service for exacerbated chronic obstructive pulmonary disease patients under the frame of a properly designed cost-effectiveness analysis.

Appendix: Description of the intervention in the home hospitalisation group

Assessment on ER admission by the specialised team

1. Characteristics of the exacerbation, comorbidities, and response to treatment at the ER
   - 1.1. Baseline conditions of the patient (duration 1.5 h): a) health-related quality of life; b) healthcare resources in the previous year; c) fragility risk factors; and knowledge of the disease and compliance to therapy.
   - 1.2. Decision on discharge from the ER or after a short period of inpatient hospitalisation based on 1.1. and 1.2.

2. Treatment at discharge
   - 2.1 Pharmacological therapy of COPD and comorbidities
   - 2.2. Nonpharmacological treatment (duration 2 h): a) education on knowledge of the disease; adherence to treatment; and recognition/prevention of triggers of exacerbation; b) selection of appropriate equipment at home; training on administration of pharmacological treatment; c) smoking cessation; d) patient empowerment on daily life activities: hygiene, dressing, household tasks; leisure activities; breathing exercises; and, skeletal muscle activity; e) nutrition recommendations; and f) socialisation and changes in lifestyle.

3. Home hospitalisation and 8-week follow-up
   - 3.1. First nurse visit at home at 24 h (duration 1 h)
     a) Assessment of the response to pharmacological treatment
     b) Introduction of changes under remote physician′s supervision
     c) On-site assessment of fragility factors
     d) Action plan revisited and education reinforced
   - 3.2. Eight-week follow-up
     a) Number of home visits and duration of HH were decided by the nurse
     b) Patient free-phone access to the nurse was ensured
     c) Nurse phone calls to patient to reinforce the action plan
   - 3.3. Failure of the programme
     a) More than five nurse home visits during the 8-week follow-up
     b) New problem requiring ER admission

4. Assessment after 8-week follow-up (see text)

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Manuscrito 2

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ORIGINAL PAPER

The impact of home hospitalization on healthcare costs of exacerbations in COPD patients

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Abstract Home-hospitalization (HH) improves clinical outcomes in selected patients with chronic obstructive pulmonary disease (COPD) admitted at the emergency room due to an exacerbation, but its effects on healthcare costs are poorly known. The current analysis examines the impact of HH on direct healthcare costs, compared to conventional hospitalizations (CH). A randomized controlled trial was performed in two tertiary hospitals in Barcelona (Spain). A total of 180 exacerbated COPD patients (HH 103 and CH 77) admitted at the emergency room were studied. In the HH group, a specialized respiratory nurse delivered integrated care at home. The average direct cost per patient was significantly lower for HH than for CH, with a difference of 810€ (95% CI, 418–1,169€) in the mean cost per patient. The magnitude of monetary savings attributed to HH increased with the severity of the patients considered eligible for the intervention.

Keywords COPD · Healthcare costs · Healthcare delivery · Homecare · Hospitalization

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Introduction

Hospital admissions related to acute exacerbations of chronic obstructive pulmonary disease (COPD) have a deleterious impact on health related quality of life and on mortality risk in these patients. Moreover, the burden of exacerbations for the entire health system is high [1], both from an economic and organizational point of view [2, 3]

The overall economic burden of COPD (direct and indirect costs) has been estimated as being equivalent to 0.32% of US gross domestic product in 2001, and direct medical costs attributed to COPD accounted for 1.5% of US healthcare expenditure [4]. Empirical evidence in many countries showed that expenditures for COPD patients are more than 2.4 times that of all healthy insured population [2]. Moreover, expenditure for hospitalizations represent >70% of all COPD-related medical care costs [5].

There has been controversy regarding the effects of home hospitalization (HH) schemes on costs. Two

randomized controlled trials [6, 7] reported that HH significantly increased healthcare costs for COPD patients [8]. However, four controlled trials conducted in the United Kingdom [9–11] and in Barcelona (Spain) [12] have shown both safety and cost reductions when these type of services, either HH directly from the emergency rooms or early discharge from the hospital, are applied to appropriately selected COPD patients with a well-defined intervention at home.

Using the same data set reported by Hernandez et al. [12], the current analysis assessed whether HH is associated with lower direct health care costs than conventional hospitalization (CH). The main objectives of the current study were: (1) to determine the marginal impact of HH, in comparison with CH, on direct patient health care costs; and (2) to predict health costs of exacerbated COPD patients conditional on individual disease severity and treatment characteristics, including the intervention (HH).

Methods

Study design

Over a 1-year period (1 November 1999 to 1 November 2000), 222 patients with COPD exacerbations were included in the study among those admitted at the emergency room (ER) of two tertiary hospitals (Hospital Clínic and Hospital Universitari de Bellvitge) of Barcelona, Spain. The two primary criteria for inclusion in the study were: (1) COPD exacerbation as major cause of referral to the ER; and (2) absence of any criteria for imperative hospitalization as stated by the British Thoracic Society (BTS) guidelines [4] (i.e., acute chest X-ray changes; acute confusion; impaired level of consciousness; and arterial pH below 7.35). Patients that agreed to participate were randomly allocated to either the intervention group (HH) or the control group (CH). A detailed description of the study groups (HH and CH), characteristics of the intervention, and generalities of the cost analysis are reported in Hernández et al. [12].

One hundred and sixty-five (26.2%) of the 629 screened patients required imperative hospitalization. Two hundred and twenty patients showing at least one exclusion criteria (not living in the health care area or admitted from a nursing home; lung cancer and other advanced neoplasms; extremely poor social conditions; severe neurological or cardiac comorbidities; illiteracy; no phone at home) were not considered in the program. Up to 244 patients (38.8%) were considered eligible for the study, but 22 subjects (3.5%) did not sign the informed consent after full explanation of the characteristics of the protocol. The remaining 222 patients (35.3%) were blindly assigned using a set of computer-generated random numbers in a 1:1 ratio either to the treatment group (home-based hospitalization (HH)) or to the control group (conventional care) [12]. One of the hospitals used a 2:1 randomization ratio during the first 3 months of the study, which explains the difference in number between the two groups.

Intervention group

A specialized team assessed only patients assigned to HH. For each HH patient, the nurse scheduled a first home visit within 24 h after discharge. The respiratory nurse set the length of the HH. A maximum of five nurse visits at home were permitted during the 8-week follow-up period, but patient's phone calls to the nurse were not limited in number. The intervention was considered to be a failure if one of the two following events occurred: the patient relapsed and required referral to the ER, or >5 nurse visits at home were needed during the follow-up period. In both circumstances, the patients were analyzed in the study, but they were not considered for a new randomization (i.e., when attended at the ER for the relapse).

The HH intervention had three main objectives: (1) an immediate or early discharge from the hospital was encouraged by the specialized team aiming to either avoid or reduce the length of inpatient hospitalization; (2) a comprehensive therapeutic approach was tailored on an individual basis, according to the needs detected by the specialized team; and (3) patient support by a skilled respiratory nurse either through home-visits or free-phone consultation was ensured during the 8-week follow-up period.

Control group

Patients included in the conventional care group (controls) were evaluated by the attending physician at the ER who decided either on in-patient hospital admission or discharge. Pharmacological prescriptions followed the standard protocols of the centers involved in the study that were similar in the two groups, but the support of a specialized nurse at the ER and at home was not provided to controls. At discharge, the patient was usually supervised by the primary care physician who was not aware of the protocol.

In the present study, sample size was reduced to 180 patients (HH 103 and CH 77). The remaining 42 patients were excluded from the cost analysis and

subsequent multivariate linear regression models: 12 patients died during the follow-up, 16 patients had missing data in the dependent variable (total cost), and 14 patients had missing data in some potential explanatory variables (socio-demographic, clinical or functional data).

Measurement and valuation of resources

Costs were calculated for each group from the perspective of the public insurer, such that, the cost analysis was restricted to direct healthcare costs; patient time and informal care were not evaluated in this study.

The categories to be considered to estimate the cost at individual patient level were: (1) hospital length of stay (days of initial hospitalization plus days during hospital re-admissions); (2) emergency room visits not requiring admission to the hospital; (3) hospital outpatient visits to specialists; (4) primary care physician visits; (5) visits for social support; (6) nurse visits at home; (7) ambulatory treatment prescriptions; (8) phone calls; and (9) transportation services. Data on use of categories were obtained for each patient during the follow-up period.

Independently of the type of resource, individual costs for each patient have been calculated according to the initial assignment to the HH or the CH group. Real savings in the number of each type of resource (hospitalization, visits, drugs, etc.) have been reported in a previous paper [12].

The total cost for each category was calculated as the product of the number of events times the unit cost per event (i.e., hospitalization costs were calculated as days in hospital including initial stay plus readmissions times the average hospitalization cost per day). Unit costs are expressed as year 2000 prices using euros (€). Costs for nurse visits at home, ambulatory drug prescriptions, phone calls and transportation services were directly calculated using information about labor cost, market prices including value added tax, and overhead costs. Hospital unit costs per in-hospital stay and visits were calculated as average observed tariffs for COPD patients in a public insurance company covering the civil servants of the City Council of Barcelona (PAMEM). These tariffs are mainly paid to public and non-profit hospitals and they represent an adequate basis for estimation of costs in the current study given that our interest is in the financial costs for third party insurers. Calculation of costs for individual COPD patients included in the randomized controlled trial followed quality recommendations for costing in the health economics literature [13].

Statistical analysis

We computed the difference in the mean cost per patient between treatment groups. Because cost data were non-normally distributed, a 95% confidence interval (95% CI) was estimated by the re-sampling technique of bootstrapping. We estimated confidence intervals for the mean of all the cost variables included in the model using the bias-corrected and accelerated (BCa) confidence interval with 1,000 bootstrap replicates of the same original sample size [13]

We estimated a multivariate cost function to evaluate the average marginal contribution of the HH on healthcare costs using total cost as the dependent variable, and some explanatory variables plus the intervention (HH or CH) as independent variables. Potential explanatory variables to be included in the multivariate cost function were selected from the results of the comparisons carried out between the two groups (HH and CH) plus those variables included according to the observation of their potential predictive value of COPD costs in the literature. The latter was completed surveying the results of an extensive bibliographic search (Medline and Cochrane Library) for the terms ''COPD exacerbations'', ''health care costs'', and ''economic evaluation''.

Several empirical specifications for the cost function were considered: (1) without log transformation of cost, (2) with log transformation of cost, and (3) with log transformation of cost with bias correction. We decided to use the log transformation of the dependent variable, because the total cost (dependent variable) is badly skewed to the right, and a scale transformation is needed to normalize data and obtain more precise and robust estimates. However, the scale of ultimate interest is the original scale, thus back-transformation was done. The re-transformation yields a biased estimate of the arithmetic mean of the distribution of predicted cost per patient [13]. To correct for this bias, we used the smearing estimator [13]. The study of correlation and the multicollinearity between variables, and normality and heteroscedasticity tests were performed.

Predictive validity is examined within the entire test sample. As the mean expected cost per patient is the statistical of interest, the validation criteria based on the root mean square error (RMSE) are proper for choosing between the three competing models [14]. Using the best model, the one with the minimum RMSE score, the expected cost for a given patient type was calculated.

Results

Factors determining mean cost per patient

The mean overall patient costs were 1,154€ for HH and 1,964€ for CH. Table 1 indicates the 2.5 and 97.5 percentiles for the mean patient cost of HH (95% CI, 923–1,452€) and CH (95% CI, 1,573–2,621€). A difference in favour of HH amounting to 810€ (95% CI, 418–1,169€) in the mean cost per patient was observed.

The main factors contributing to this cost difference were in-patient hospital stays (846 vs 1,713€, HH and CH, respectively), pharmaceutical ambulatory prescriptions (220 vs 176€), nurse home visits (40 vs 0€), phone calls (20 vs 0€), and emergency room visits (10 vs 28€). No statistically significant differences between groups were observed in the average cost of outpatient visits, primary care physician visits, social support visits, and transport.

It is of note, that in-patient hospital stays were the main input contributing to mean cost per patient in the two groups (HH and CH) of exacerbated COPD patients. The proportion of hospital stays cost on overall patient cost was 87% in CH, and it only decreased to 73% in HH. Thus, HH was cheaper than CH by 867€ (95% CI, 719–1,184€) for the mean in-patient hospital stay cost per patient observed in our study.

Pharmaceutical ambulatory cost represented 9% of mean CH patient cost and 19% of mean HH patient cost. Mean pharmaceutical ambulatory cost per patient was significantly higher in HH than in CH, with a difference of 44€ (95% CI, 40–49€) per patient. However, given that this study is not able to distinguish the utilization of drugs inside the hospital, differences in drug expenditure only refer to ambulatory drug consumption, and overall differences in drug consumption cannot be well established. Main characteristics of HH and CH are compared in Table 2. This analysis was done to identify potential explanatory variables to be included in the multivariate cost function model.

Multivariate cost function

The comparison of the three competing multivariate regression models alluded to in Methods showed the lowest RMSE (1,564€) for the log-transformed linear model with bias correction (*smearing estimator*) which was adopted in the current study. Alternatively, the RMSE values for the linear model and for the model with log-transformation model without bias correction were 1,590 and 1,690€, respectively. Table 3 indicates the covariates included in the multiple regression analysis and the corresponding estimated coefficients. Four variables predicted the total cost: (1) FEV_1, expressed as percent of predicted value; (2) health related quality of life, expressed as the total score of Saint George's Respiratory questionnaire (SGRQ); (3) the number of COPD exacerbations requiring in-hospital admission in the previous year; and (4) the intervention (HH). As shown in the table, high SGRQ total score (poor health related quality of life), high number of in-hospital admissions during the previous year and low FEV_1 were independently associated with higher costs. In contrast, HH was related to lower costs independently of any effect associated with other potential explanatory factor.

Table 1 Mean average health care cost per patient, according to treatment group

Categories	Home hospitalization (n = 103)					Conventional hospitalization (n = 77)				
	% of zeros	Skewness	Mean	BCa's percentiles		% of zeros	Skewness	Mean	BCa's percentiles	
				2.5%	97.5%				2.5%	97.5%
In-patient hospital stay	34.00	2.809	846.07	627.59	1,130.13	11.70	2.942	1,713.38	1,346.31	2,313.72
Emergency room visits	90.30	3.449	10.06	4.64	16.25	75.30	1.678	27.95	18.63	40.37
Outpatient visits	90.3	3.458	4.64	2.32	7.74	85.70	8.252	24.84	7.25	94.32
Primary care physician visits	96.1	7.139	4.61	0.92	12.89	89.60	4.072	9.25	3.70	17.36
Social support visits	98.1	8.105	0.55	0.00	2.06	94.80	5.657	2.68	0.73	7.63
Nurse home visits	14.6	0.343	40.11	35.19	45.52	–	–	–	–	–
Ambulatory prescriptions	0.0	0.123	219.96	204.59	235.88	0.00	0.016	175.54	155.28	195.66
Total phone calls	16.5	1.291	20.22	17.16	23.80	–	–	–	–	–
Transport	33.0	1.054	8.11	6.83	9.82	27.30	1.283	10.62	8.59	13.13
Average direct cost per patient	0.0	2.838	1,154	923	1,452	0.00	2.812	1,964	1,573	2,621

Costs are expressed in euros at year 2000 prices

% of zeros refers to the proportion of patients without hospitalization

Table 2 Comparison of sociodemographic and health characteristics of the intervention and control groups

	Home hospitalization (n = 103)	Conventional hospitalization (n = 77)	Total patients (n = 180)
Sex[a]**			
Female	2 (1.9)	2 (2.6)	4 (2.2)
Male	101 (98.1)	75 (97.4)	176 (97.8)
Age (years)[b]**	70.8	70.7	70.8
Marital status[a]**			
Married or living in pair	79 (76.7)	51 (66.2)	130 (72.2)
Unmarried, divorced, separated or widowed	24 (23.3)	26 (33.8)	50 (27.8)
Labor situation[a]**			
Working	15 (14.6)	8 (10.4)	23 (12.8)
Not working	88 (85.4)	69 (89.6)	157 (87.2)
Studies[a]**			
Primary	90 (87.4)	68 (88.3)	158 (87.8)
Secondary or university	13 (12.6)	9 (11.7)	22 (12.2)
Annual income[a]**			
≤12,000€	86 (83.5)	65 (84.4)	151 (83.9)
>12,000€	17 (16.5)	12 (15.6	29 (16.1)
PaO_2 (mmHg)[b]**	66.06	65.23	65.71
$PaCO_2$ (mmHg)[b]**	42.26	43.94	42.98
FEV_1 (% predicted)[b]**	43.0	39.2	41.4
FEV_1/FVC (%)[b]**	50.0	50.7	50.3
Dyspnoea score (VAS)[b]**	6.3	6.3	6.3
Co-morbidity[a]**			
Yes	96 (93.2)	75 (97.4)	171 (95.0)
No	7 (6.8)	2 (2.6)	9 (5.0)
No. of chronic upsets[b]**	2.88	3.13	2.99
Exacerbations requiring in-hospital admission in the previous year[b]**	0.56	0.91	0.71
Exacerbations requiring emergency room admission in the previous year[b]**	0.55	0.89	0.70
Total SGRQ score[b]**	51.8	46.4	49.5
Physical summary SF-12 score[b]*	37.0	34.3	35.9
Mental summary SF-12 score[b]**	44.3	43.2	43.9
Vaccination in previous year[a]**			
Yes	68 (66.0)	49 (63.6)	117 (65.0)
No	35 (34.0)	28 (36.4)	63 (35.0)
Current smoker[a]**			
Yes	27 (26.2)	13 (16.9)	40 (22.2)
No	76 (73.8)	64 (83.1)	140 (77.8)
Respiratory rehabilitation exercises in the previous 4 weeks[a]**			
Yes	10 (9.7)	7 (9.1)	17 (9.4)
No	93 (90.3)	70 (90.9)	163 (90.6)
Compliance on oral medication[a]*			
Yes	42 (40.8)	42 (54.5)	84 (46.7)
No	61 (59.2)	35 (45.4)	96 (53.3)
Compliance on inhalation therapy[a]**			
Yes	63 (61.2)	50 (65.0)	113 (62.8)
No	40 (38.8)	27 (35.0)	67 (37.2)
Clinical outcomes (8-week follow-up)			
Inpatient hospital readmissions (number of episodes)[b]*	0.24 (0.57)	0.38 (0.70)	0.30 (0.62)
Emergency room readmissions (number of episodes)[b]*	0.13 (0.43)	0.31 (0.62)	0.21 (0.51)

Results are expressed either as mean or number of subjects in the corresponding category. Percentage of subjects is expressed within brackets. Annual income, expressed in euros at year 2000 prices

PaO_2 partial pressure of oxygen, $PaCO_2$ partial pressure of carbon dioxide, FEV_1 forced expiratory volume during the first second, FEV_1/FVC ratio, *VAS* visual analogical scale for scoring dyspnoea, *SGRQ* Saint-George's respiratory questionnaire, *SF*-12 questionnaire

*$P > 0.05$; **$P > 0.1$

[a] Chi-square test

[b] *U* Mann–Whitney non-parametric test for independent samples

Home hospitalization savings and disease severity

We estimated the costs per individual patient for four different degrees of disease severity, as indicated in Table 4 and Fig. 1. Given the regression model chosen in the current study, a back transformation and smearing was needed to estimate the expected cost per patient [15]. The so-called ''average'' patient was

Table 3 Multivariate estimate of patient costs

Dependent variable log (cost)		
Explanatory variables	Estimated coefficient (OLS)	Standard error
Constant	6.979586	0.294397**
FEV1	–0.009642	0.004817*
Total SGRQ score	0.006030	0.002978*
Exacerbations requiring in-hospital admission in the previous year	0.169333	0.072935*
Intervention group (HH = 1)	–0.406642	0.160144*
Smearing factor	1.5811	
R^2	0.138	
Adjusted R^2	0.118	

FEV1 forced expiratory volume during the first second at 8 weeks of follow-up, *Total SGRQ score* total Saint George Respiratory Questionnaire score, *HH* home hospitalization

*$P < 0.01$; **$P < 0.05$

defined by values of each covariate equal to the sample mean values. The estimated cost for the ''average'' COPD patient was 1,154€ with HH and 1,801€ with CH. In other words, estimated savings attributable to the intervention (HH) in this hypothetical patient were 647€.

It is noteworthy that differences in cost due to HH increased when disease severity augmented. Cost savings were 458€ for a light COPD patient, 775€ for a moderate COPD patient, and 1,419€ for the highest disease severity considered in the analysis.

Discussion

A cost minimization analysis

In the current study, we demonstrated that HH decreased direct patient health cost by –36% cost in comparison to CH. The results obtained from the multivariate cost function clearly provide a useful insight on the efficiency gains than can be expected from integrated home care programs in the management of COPD exacerbations. The multivariate cost function has proven to be useful for disease cost forecasting and for evaluation and budgeting purposes.

In a previous paper using data from the same randomized controlled trial [12], a noticeable improvement in quality of life ($P = 0.03$) and in other clinical outcomes was demonstrated. But differences between HH and CH in most clinical outcomes disappeared when a more stringent threshold ($P = 0.01$) was adopted. In the current study, we assumed no differences in clinical outcomes between HH and CH [16]. Then, we might consider that the two alternative programs may be viewed as equivalent in outcome and adopt the simple approach of a cost-minimization analysis [17]. Under this approach, this paper tested the primary economic hypothesis of weak dominance. That is, HH showed similar safety and effectiveness than CH, but the former was less costly. The results of the current analysis were consistent with this hypothesis. The average marginal impact of the intervention (HH) in comparison with CH represented a mean cost saving of 647€ per patient ($P < 0.01$).

Limitations of the current evaluation

The economic evaluation performed in the present study may be affected by several limitations. First, the perspective of the evaluation was that of the public healthcare insurer, excluding non-health care costs. However, the short time horizon of the study (8-week follow-up) and the high cost of COPD exacerbations could be an indication of a possible small proportion of total cost for resources not included in the analysis. In this study, formal (paid work) or informal (unpaid work and leisure time) care for exacerbated COPD patients were not evaluated. Notwithstanding, a

Table 4 Expected cost per patient for different levels of disease

Patient type	Variables values according to severity levels			Predicted cost by intervention group		Savings[a]
	FEV_1	Total SGRQ score	Admissions previous year (number)	HH	CH	
Slight	70	35	1	842.4	1,300.3	457.8 (143.6–685.7)
Moderate	50	55	2	1,364.7	2,139.3	774.5 (265.7–1,143.6)
Severe	30	85	3	2,348.3	3,767.4	1,419.1 (543.5–2,054.2)
Average	41.40	49.5	0.71	1,153.7	1,800.9	647.1 (216.9–959.1)

Costs are expressed in euros at year 2000 prices. The smearing estimator has been applied

FEV1 forced expiratory volume during the first second at 8 weeks of follow-up, *Total SGRQ score* total Saint George Respiratory Questionnaire score, *HH* home hospitalization, *CH* conventional hospitalization

[a] 95% confidence interval

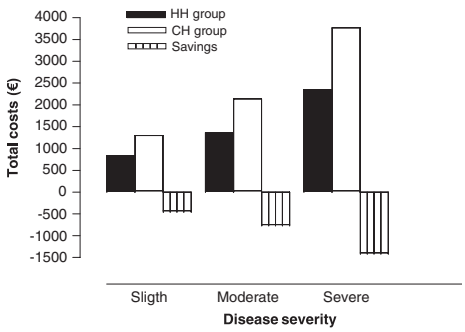

Fig. 1 Total costs predictions as expressed by different levels of disease severity. Home hospitalization intervention (*HH*) was cheaper for any level of disease severity and severely ill patients obtained largest savings. *CH* Conventional hospitalization

previous randomized controlled trial comparing hospital-at-home care with inpatient care [6] reported that carers' expenses made up a small proportion of total costs and inclusion of these costs did not alter the results.

A second limitation is that average costs were used to value hospital care. In fact, the existence of fixed hospital costs could amplify the value of any potential savings resulting from a reduction in bed-days. Another limitation related to the use of average cost to value hospital care is that normally the first days in a hospital are more expensive than the later days. A third limitation of the present evaluation comes from the fact that the clinical outcomes refer to a short-period of time, given that the time horizon is restricted to the 8-week follow-up. In fact, there is no evidence of persistence of these results over a longer period of time.

Implications for healthcare policy

In conclusion, the current study demonstrates that a well defined home-based integrated care program for the management of COPD exacerbations is of interest, even if we adopt the weak dominant alternative, as assumed in the cost minimization analysis carried out in the present analysis.

Patients assigned to HH should be assessed according to well-established criteria in order to guarantee that clinical outcomes, safety and costs of HH are maintained as promised. In this sense, the results obtained in this study only apply to the subgroup of patients with a COPD exacerbation as a major cause of referral to the ER, and in the absence of any criteria for imperative hospitalization as stated by the BTS guidelines. Also, external validity is heavily dependent on the design of the HH protocol under identical conditions to those employed in the study reported in this paper [12].

A potentially relevant policy-related implication of the current results could arise from the fact that the magnitude of resource savings under HH is higher when the intervention is applied to more severely exacerbated COPD patients. Such a statement might be controversial, and probably deserves more attention and future research. Notwithstanding, we need to point out three considerations. First, it has been well established in the clinical literature that COPD costs are positively correlated with disease severity. Then, absolute savings could be higher in the provision of efficient management of more severe COPD patients. Second, the largest savings for more severe patients could be arbitrarily imposed by the empirical specification of the cost function, given that, since the dependent variable is log-transformed, the retransformation yields an exponential increase. And, third, the result only holds for more severely exacerbated COPD patients among those eligible for the HH program, i.e., excluding some of the more severely ill COPD patients.

Hospital at home should be analyzed in the context of chronic disease care, in the so-called chronic care model [18, 19]. The identification of patients at high risk, the cooperation among primary care and specialists, the focus on social care, and the investment in information technology could improve chronic care [20]. The data of present study suggest that severe COPD patients with social support could reach the highest benefits of home-specialized care.

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Manuscrito 3

Early Relapses After Severe Exacerbations in Patients with Chronic Obstructive Pulmonary Disease
(Submitted)

EARLY RELAPSES AFTER SEVERE EXACERBATIONS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Exacerbated COPD patients requiring emergency room admission show high rates of early relapse. We analyzed independent predictors of re-admissions in 222 exacerbated COPD patients (71±10 (SD) yrs) randomly assigned either to home hospitalization (HH, n=121) or conventional care (CC, n=101). After 8 weeks follow-up, HH showed better outcomes at lower cost than CC. Lung function, health related quality of life, four items of the British Thoracic Society questionnaire (general condition, home bound, breathlessness and physical activity) and number of severe exacerbations during the previous year were predictors of relapse. The final logistic model included: poor general condition (OR 3.72, p= 0.005), severe breathlessness (OR 3.07, p= 0.03), SF-12 physical summary component (OR 0.96, p= 0.05), hospitalizations during the last year (OR 1.23, p= 0.17) and FEV_1 % predicted (OR 0.99, p= 0.23). A separate analysis of the explanatory role of the changes during the follow-up showed that increased physical activity (OR 0.176, p= 0.001) was associated with lower re-admission rates. The study identifies easily obtainable variables that may help the decision making process in severe exacerbations. Our results reinforce the positive role of enhanced physical activity after discharge and prompt novel hypotheses to explain a poor outcome in these patients.

Key words: COPD; Exacerbations; Home care; Hospitalization; Physical activity

INTRODUCTION

Patients with severe exacerbations of chronic obstructive pulmonary disease (COPD) requiring emergency room (ER) or hospital admission show high rates of early relapses after discharge. In developed countries, approximately one third of these patients use to require re-admission within 2 months[1-5]. Observational studies on severe exacerbations of COPD[6-8] indicate that the degree of functional impairment together with repeated hospital admissions in the previous year are the two most important factors associated with unplanned hospitalizations. Moreover, repeated hospital admissions are usually associated with poor health related quality of life (HRQL)[9;10], accelerated functional decline[11;12], and increased mortality[13].

We hypothesize that the scenario described above can be partly explained by two complementary factors. First, management strategies for COPD patients presently in place must be revisited in the light of new modalities of healthcare[14] aiming to overcome the problems associated with fragmented care in chronic patients[15-19]. Second, but not less important, pivotal underlying mechanisms that modulate the natural history of the disease are not properly taken into account in the clinical management of these patients. A constellation of studies suggest that factors poorly related with impairment of FEV_1 play an important role on disease outcomes. Namely, the association between aerobic capacity (maximum O_2 uptake) and survival[20] and the relationships between poor physical activity and hospitalization rate[8], let alone the impact of cell oxygenation on systemic effects of the disease[21].

In a recent study[22], conducted in 222 exacerbated COPD patients admitted at the ER of two tertiary hospitals in the area of Barcelona, we showed that home

hospitalization (HH) of selected patients with free phone access to a specialized respiratory nurse through a call center generated a better outcome (lower rate of ER relapses and higher improvement of HRQL) with lower direct costs and higher patient's satisfaction than conventional in-patient hospitalization. These results were explained by better self-management of the disease due to behavioral improvement[22] and less anxiety of the patients due to expanded accessibility to the healthcare system with the support of information and communication technologies[23].

The aims of the current study, conducted with data collected prospectively in our previous investigation[22] were twofold. Firstly, to identify the factors associated with early relapses in exacerbated COPD patients. The purpose of this investigation was to generate sufficient information that could help to improve the selection of candidate patients for home-based programs. An ancillary analysis of the changes observed during the 8-week follow-up period was also done to explore potential associations with early relapse. In the present study, early relapse was defined as hospital or ER re-admissions within the 8 week follow-up period, including deaths.

METHODS

Study Groups

Two hundred and twenty two COPD patients were included in the study among those admitted at the ER of two tertiary hospitals over one-year period[22]. Briefly, the two primary criteria for inclusion in the study were: COPD exacerbation as major cause of referral to the ER[24], and absence of any criteria for imperative hospitalization as reported elsewhere[4;22]. Six hundred twenty nine patients (n= 629) were screened by a specialized respiratory team in the ER but only 35.3% complied with inclusion criteria. Finally, 121 patients were randomly assigned to HH and 101 patients were treated through conventional hospital care (CC).

Interventions

In the HH group, immediate or early discharge from the hospital was encouraged by the specialized team aiming to either avoid or reduce the length of in-patient hospitalization. For these patients, a comprehensive therapeutic approach was tailored on an individual basis, including education on self-management of the disease[15;22;26]. Patient's support by one skilled respiratory nurse through home visits and free-phone consultation was ensured during the 8-week follow-up period[22].

Patients included in the CC group were evaluated by the attending physician at the ER who decided either to admit the patient in the hospital or to discharge her/him with usual care. Pharmacological prescriptions followed the standard procedures of the centers involved in the study and were similar in the two groups of patients (HH and CC).

Assessment and Follow-up

Assessment was blind for the two subsets of patients and included: evaluation of the British Thoracic Society (BTS) questionnaire of severity of the exacerbation[25] and administration of extensive questionnaires at baseline and 8-weeks after follow-up, as reported in detail previously [7;22;26]

Statistical Analysis

Results are expressed as mean(SD) or n[%], as appropriate. Comparison of baseline information and changes after follow-up between the two groups (with and without early relapse) were done as described in the tables.

A multivariate logistic regression analyses was performed in order to identify predictors of early relapse (dependent variable) at baseline. Upon completion of the univariate analyses, all baseline factors with a univariate test p value < 0.25 and those variables that had been considered *a priori* as clinically relevant (**Table 1**) were considered candidates for the multivariate model. Before the logistic regression model was built, collinearity among candidate variables was assessed with the calculation of the variance inflation factor (VIF). A VIF above 2.5 for a given variable was taken as an indication of co-linearity problems with other(s) variable(s)[27] in the study. Unless the variable was considered *a priori* as clinically relevant, it was excluded from the logistic regression analysis. A sequential approach was used to select the final variables to be included in the logistic model. Each variable was assessed by examining its statistical significance and possible confounding effects with other variables. Independent variables that did not contribute to the fit to the model based in these two criteria were eliminated and a new model was fit. A first predictive model was estimated including only clinical and socio-demographic variables. In a second step, a complete predictive model was built adding both BTS and HRQL variables to the first model.

A separate logistic analysis was carried out with explanatory purposes. In this analysis, changes observed during the follow-up period were also included.

Statistical significance was accepted at p values < 0.05. Goodness of fit of the final models was assessed with the Hosmer-Lemeshow (HL) test and the area under the receiver operating characteristic (ROC) curve. All analyses were performed using SPSS version 10.0 for Windows and SAS™ software, Version 8 of the SAS System for Windows[28].

RESULTS

Seventy nine (36%) out of the 222 patients presented relapses during the 8-week follow-up period, defined as inpatient re-admissions (n= 49, 22%), ER re-admissions (n= 32, 14%) and/or deaths (n= 12, 5%). Univariate comparisons of socio-demographic characteristics, risk factors, clinical status, lung function variables, HRQL and indicators of appropriateness of treatment were done between patients with early relapses and those who showed a successful outcome. Baseline characteristics of

patients with early relapses and those who showed a successful outcome are shown in **Table 1** for those variables considered in the multivariate analyses described below. The detailed list of all variables in the study are reported in reference[22]. Patients with a successful outcome were slightly younger (p= 0.02), predominantly fell into the HH treatment (p= 0.02) while showing lower number of hospital admissions in the previous year (p< 0.01) than those patients with relapses. Patients with successful outcome exhibited higher FVC (p= 0.003) and FEV_1 (p= 0.002) and slightly lower $PaCO_2$ (p= 0.03) than those with early relapse. Moreover, HRQL assessed by both SGRQ and SF-12 questionnaires[29;30] was better in patients without relapses. It is noteworthy that several items of the BTS questionnaire showed significant differences between the two groups. Namely, poorer general condition, poorer ability to cope at home, more severe breathlessness and poorer physical activity (p< 0.01 each) in patients with relapses.

Predictors of early relapse

The logistic regression model shown in **Table 2** identifies the independent predictors of early relapse at baseline. In order to assess the association of clinical and lung function variables with early relapses, a logistic regression analysis was performed including the previously identified variables falling into these two categories, together with the socio-demographic variables. As displayed in **Table 2**, left column, the number of admissions in the previous year and FEV_1 % predicted were the only statistically significant variables.

A second step in the analysis included HRQL information and the relevant variables of the BTS questionnaire (**Table 2**, right column) which provided the final prediction equation. As indicated in the table, two items of the BTS questionnaire, *i.e.* poor general condition (OR 3.72, p= 0.005) and severe breathlessness (OR 3.07, p= 0.03); and the SF-12 physical summary component (OR 0.96, p= 0.05) were the main predictors of relapse. Despite the fact that adjustment by HRQL and the BTS questionnaire removed the statistical significance of the number of hospitalisations in the previous year and FEV_1 % predicted, these two variables were also included in the final model because of their clinical relevance.

In all analyses, FEV_1 showed high co-linearity with $PaCO_2$ such that both descriptors (FEV_1 and $PaCO_2$) were interchangeable without a significant impact in the coefficients of the remaining variables included in the model. A strong co-linearity was also observed among the BTS variables showing statistical significance in the univariate analysis (**Table 1**). The latter were poor general condition, poor ability to cope at home, severe breathlessness, and poor physical activity.

The HL goodness of fit test corresponding to the final model was 5.98, with a p value of 0.65, indicating that the model was well calibrated. Moreover, the area under the ROC curve (0.74) indicated that the model properly discriminated between patients with early relapse and those with successful outcome.

Eight-week follow-up period

While patients with early relapse did not show clinically (nor statistically) significant improvements in the SGRQ during the 8-week follow-up period (ΔSGRQ total score, 2.1±12.2) (**Table 3**), all SGRQ dimensions significantly improved in patients with a successful outcome (ΔSGRQ total score, -8.2±14.3). Likewise, significant differences between the two groups were also found in the change in dyspnea score (p< 0.01) and in enhancement of the SF-12 physical summary component (p< 0.01). The oxygenation index (PaO_2/F_IO_2) significantly improved in patients with successful outcome (by 34±63 mmHg; baseline PaO_2/F_IO_2 295±61 mmHg), as opposed to the absence of change in those with early relapse (by 6±73 mmHg; baseline PaO_2/F_IO_2 301±68 mmHg). Moreover, enhancement of both inhalation technique (p= 0.036) and improvement of physical activity (p= 0.001) also showed significant differences between the two subsets of patients.

In order to speculate on explanatory mechanisms for the high rate of unsuccessful outcome in these patients, we examined the association between early relapse (dependent variable) and the changes observed during the 8-week follow-up period (**Table 4**). The logistic model included as covariates: predictors at entry (**Table 2**), treatment group (HH or CC) and the observed changes during the follow-up reported in **Table 3**, except ΔHRQL variables. **Table 4** displays the results adjusted by treatment group and appropriateness of treatment. It is of note that among all changes during the follow-up alluded to above (**Table 3**), only the increase in physical activity after discharge showed a significant explanatory role (OR 0.176, p= 0.001), followed by arterial oxygenation improvement (OR= 0.99, p= 0.081) which almost reached statistical significance.

DISCUSSION

The 2003 GOLD update[31] acknowledges that nurse administered home care represents an effective and practical alternative to conventional hospitalisation in selected non-acidotic patients with COPD exacerbations. GOLD[32], however, was unable to provide specific recommendations due to the absence of information on criteria for indication of HH in these patients. To our knowledge, the current study constitutes the first attempt to identify independent predictors of early relapse taking into account this modality of care. While demonstrated cost efficacy and safety of the intervention[22], the current study did not show influence of the modality of care on the type of predictors of relapse. An added value of the present investigation is the fact that it was done in a well identified group of COPD patients in whom the effects of the intervention (HH) were extensively assessed[22] and compared with those described by other authors. This fact is counterbalanced, at least in part, by inherent methodological constraints for further completing the predictive analysis due to the inclusion of both the intervention (HH) and control (CC) groups.

Besides the confirmation of the independent generic contribution of HRQL to baseline prediction of the outcomes of severe exacerbations[33], the current study identifies the predictive role of rather simple variables

easily obtainable by the BTS questionnaire at the ER. Moreover, our investigation also highlights the importance of enhanced physical activity after discharge in these patients.

Practical Implications

The current results confirm that the high rate of early relapses is a major clinical problem in the management of exacerbated COPD patients. Despite the fact that GOLD recommendations[32] were properly adopted in the two groups of patients, approximately 36% of them showed relapses as defined in the study. This figure is similar to those reported by studies carried out in different economically developed countries[1-5]. These data further strengthen the idea that reduction of early re-admissions constitutes a relevant target in order to improve patient's management [14-17]. In this regard, properly evaluated innovative home-based services appear as a key component of the strategy to prevent relapses[22].

The study proposes a prediction model (**Table 2**, right column) to consider in the ER assessment of these patients. An important outcome of our investigation was the identification of the predictive role of simple variables easily obtainable at the ER from the BTS questionnaire. The high co-linearity among the four BTS variables may reflect the interplay of common underlying physiological disturbances, namely, lung function impairment and systemic effects of the disease. Accordingly, those COPD patients showing the constellation of predictors alluded to above constitute a high risk population that may require a specific pattern of care after discharge in order to prevent relapses. Compared to low risk COPD patients, they may need more intensive logistic support and better respiratory nurse accessibility together with some kind of remote home monitoring. It is of note that the predictive factors identified in our study represent an independent confirmation of those documented in recent reports[6;7] that analyzed representative samples of severe COPD exacerbations requiring hospital admission in which no specific interventions were carried out which further support the results of the current study.

Hypotheses on Underlying Mechanisms

We acknowledge that the logistic regression analysis displayed in **Table 4** only indicates the independent explanatory role of the variables included in the logistic model with no implications regarding cause-effect relationships. It is striking, however, the strong association between increase in physical activity during the follow-up and low rates of early relapse. Interestingly, $\Delta PaO_2/F_IO_2$ just failed to reach significance (p= 0.081). These results are consistent with the recent report by Garcia-Aymerich et al[8] indicating that the level of physical activity has a relevant impact on hospital admissions in these patients. These authors suggested that enhanced muscle cell oxygenation, because of higher peripheral muscle blood flow associated with physical activity, and better arterial oxygenation could be concomitant factors playing a synergistic role to prevent unplanned hospitalisations. The critical interplay between ΔVO_2, Δ cardiac output and improvement of pulmonary ventilation-perfusion (V_A/Q) matching throughout the recovery period of COPD exacerbations assessed by Barberá et al[34] provides indirect support for this contention. Moreover, several pieces of evidence stress both the relevance of the complex interactions among aerobic capacity, abnormal redox potential and cytokine regulation at systemic level in these patients[35-38] to better understand the mechanisms responsible for an accelerated progress of the disease seen in those COPD patients, who appear to be candidates for repeated severe exacerbations.

In conclusion, the current study generates evidence-based data allowing a reasonable identification of target COPD patients with high risk of early relapse. Our results may facilitate elaboration of specific recommendations for home care-based programs.

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Table 1. CHARACTERISTICS OF THE STUDY GROUPS BY OUTCOME

	Early relapse n=79	**Success** n=143	**p value**
Age, years	73 (8.4)	70 (10.2)	0.02 *
Intervention			
HH group, n [%]	35 [44%]	86 [60%]	0.02 †
Risk factors			
Current smokers, n [%]	11 [14%]	40 [28%]	0.03 †
Co-morbidities, n [%]	78 [99%]	132 [92%]	0.06 †
Number of co-morbid conditions	3.3 (1.7)	2.9 (1.7)	0.20 ‡
Patients with LTOT, n [%]	17 [22%]	17 [12%]	0.08 †
Lung Function			
$PaCO_2$ mmHg	45 (8)	42 (8)	0.03 *
FVC, l [% predicted]	2.0(0.8)[56]	2.4(0.9)[65]	0.003 *
FEV_1, l [% predicted]	0.9(0.4)[36]	1.2(0.5)[45]	0.002 *
Hospital admissions *(previous year)*			
Patients, n [%]	42 [53%]	48 [34%]	0.005 †
Number of episodes	1.1 (1.5)	0.6 (1.0)	0.005 ‡
ER visits *(previous year)*			
Patients, n [%]	36 [46%]	49 [35%]	0.10 †
Number episodes	1.1 (1.6)	0.6 (1.1)	0.03 ‡
BTS questionnaire, n [%]			
Poor general condition	23 [29%]	9 [6%]	
Ability to cope at home	56 [71%]	130 [91%]	<0.01 †
Severe breathlessness	19 [24%]	9 [6%]	<0.01 †
Poor-confined to bed level of activity	31 [39%]	20 [14%]	<0.01 † 0.005
Poor social status	12 [15%]	13 [9%]	† 0.20 †
HRQL *(previous year)*			
SGRQ questionnaire:			
Total score	63.6 (17.0)	55.5 (18.1)	0.001‡
Activity domain	82.0 (17.4)	70.7 (23.1)	<0.01‡
Impact domain	55.9 (19.7)	47.9 (19.3)	<0.01‡
SF-12 questionnaire:			
Physical domain	32.7 (7.4)	37.1 (8.5)	<0.01*
Mental domain	41.8 (13.5)	45.0 (11.5)	0.08*

Results are expressed either as mean (standard deviation) or as number of subjects in the corresponding category [%]. Only variables included in the co-linearity analyses are reported, see reference[22]. HH group, home hospitalisation group. LTOT, Long-term oxygen therapy. $PaCO_2$, partial pressure of carbon dioxide. FVC, forced vital capacity. FEV_1, forced expiratory volume during the first second. BTS questionnaire. ER visits, Emergency Room visits. British Thoracic Society questionnaire of severity of COPD exacerbations. HRQL, Health Related Quality of Life. SGRQ, Saint George Respiratory Questionnaire. **t-test for comparison of two independent samples; †Chi-square test; ‡U mann-Whitney non-parametric test for independent samples.*

Table 2 . INDEPENDENT BASELINE PREDICTORS OF FAILURE

	OR	95% CI	p value	OR	95% CI	p value
FEV_1 *(% predicted)*	0.98	(0.955,0.997)	0.02	0.99	(0.96,1.01)	0.23
Previous hospital admissions, 1 yr	1.43	(1.084,1.875)	0.01	1.23	(0.91,1.66)	0.18
Poor general condition				3.72	(1.48,9.34)	0.005
Severe breathlessness				3.07	(1.11,8.47)	0.03
Physical domain *(SF-12)*				0.96	(0.92,1.00)	0.05

Summary results of the logistic regression analysis: OR, odds ratio; 95% CI, 95% confidence interval. The first column describes the logistic model obtained considering only socio-demographic and clinical data as independent variables. Area under the ROC curve= 0.68 and the Hosmer-Lemeshow test= 8.62 (p= 0.38). The second column describes the proposed logistic model including all variables. Area under the ROC curve= 0.74 and Hosmer-Lemeshow goodness of fit test= 5.98 (p-value= 0.65). See text for further explanation.

Table 3. CHANGES DURING THE EIGHT-WEEK FOLLOW-UP PERIOD BY OUTCOME

Mean Δ week 8th minus baseline	**Early relapses** n= 67	**Success** n= 143	**p value**
Dyspnea score (VAS)	2.6(3.4)	0.1 (2.9)	<0.01*
Arterial blood gases			
PaO_2 mmHg	0.4(19.6)	5.1(14.0)	0.06†
$PaCO_2$ mmHg	-0.5(8.6)	-1.9(6.3)	0.20†
PaO_2/F_IO_2 mmHg	6(73)	34(63)	<0.01†
HRQL			
SGRQ :			
Total score	2 (12)	-8 (14)	<0.01*
Symptoms	4 (21)	-14 (22)	<0.01*
Activity	3 (17)	-5.5 (19)	0.02*
Impact	1 (15)	-8 (17)	<0.01*
SF-12 questionnaire:			
Physical domain	-2 (9)	3.4 (9)	<0.01†
Treatment appropriateness, n [%]			
Inhalation technique	44 [92]	98 [99]	0.036‡
Physical activity	12 [18]	76 [48]	0.01‡
LTOT compliance (< 15 h/day)	9 [75]	16 [73]	0.081‡
Knowledge of the disease	31 [52]	74 [59]	0.24‡

Results are expressed either as mean(standard deviation) or as percentage of subjects in the corresponding category, within brackets. Only statistically significant variables in the univariate analysis are reported. Description of all variables and data of the whole study group is done in reference[22]. VAS, Visual Analogic Scale. PaO_2/F_IO_2 change in arterial oxygenation index expressed as mmHg. in mmHg. HRQL, Health Related Quality of Life. SGRQ, Saint George Respiratory Questionnaire. Treatment appropriateness, see text for further explanation.

* *U mann-Whitney non-parametric test for independent samples*

† *t-test for comparison of two independent samples*

‡ *Chi-square test*

Table 4. EXPLANATORY MODEL INCLUDING COVARIATES OF THE PREDICTIVE MODEL AND CHANGES DURING THE EIGHT-WEEK FOLLOW-UP PERIOD

	OR	95% CI	p value
FEV_1 *(% predicted)*	0.997	(0.97,1.03)	0.851
Previous hospital admissions, 1 yr	1.271	(0.90,1.08)	0.178
Poor general condition	3.504	(1.22,10.80)	0.020
Severe breathlessness	3.309	(1.08,10.17)	0.037
Physical domain *(SF-12 questionnaire)*	0.973	(0.93,1.02)	0.224
Δ Physical activity	0.176	(0.06,0.49)	0.001
Δ $Pa0_2/F_i0_2$	0.995	(0.99,1.00)	0.081

Summary results of the logistic regression analysis adjusted by intervention and appropriateness of the treatment: OD, odds ratio; 95% CI, 95% confidence interval. Area under the ROC curve= 0.80 and Hosmer-Lemeshow goodness of fit test= 3.40 (p= 0.91). See text for further explanation.

Manuscrito 4

Integrated care prevents hospitalisations for exacerbations in COPD patients
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Integrated care prevents hospitalisations for exacerbations in COPD patients

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ABSTRACT: **Hospital admissions due to chronic obstructive pulmonary disease (COPD) exacerbations have a major impact on the disease evolution and costs. The current authors postulated that a simple and well-standardised, low-intensity integrated care intervention can be effective to prevent such hospitalisations.**

Therefore, 155 exacerbated COPD patients (17% females) were recruited after hospital discharge from centres in Barcelona (Spain) and Leuven (Belgium). They were randomly assigned to either integrated care (IC; n=65; age mean±SD 70±9 yrs; forced expiratory volume in one second (FEV_1) 1.1±0.5 L, 43% predicted) or usual care (UC; n=90; age 72±9 yrs; FEV_1 1.1±0.05 L, 41% pred). The IC intervention consisted of an individually tailored care plan upon discharge shared with the primary care team, as well as accessibility to a specialised nurse case manager through a web-based call centre.

After 12 months' follow-up, IC showed a lower hospitalisation rate (1.5±2.6 *versus* 2.1±3.1) and a higher percentage of patients without re-admissions (49 *versus* 31%) than UC without differences in mortality (19 *versus* 16%, respectively).

In conclusion, this trial demonstrates that a standardised integrated care intervention, based on shared care arrangements among different levels of the system with support of information technologies, effectively prevents hospitalisations for exacerbations in chronic obstructive pulmonary disease patients.

KEYWORDS: **Chronic obstructive pulmonary disease, healthcare delivery, information technology, integrated care, planned care**

Chronic obstructive pulmonary disease (COPD) generates a significant burden on healthcare systems worldwide [1, 2]. Hospital admissions due to exacerbations [3] are a major problem in the management of the disease due to their negative impact on health-related quality of life [4, 5], prognosis and costs [6, 7].

Unlike other chronic conditions [8, 9], efficacy of interventions aimed at preventing hospitalisations due to exacerbations in clinically stable COPD patients is controversial [10–13]. While two randomised controlled trials [12, 13] failed to show positive effects, the Quebec study [10] reported effectiveness of patient empowerment for self-management in moderate-to-severe COPD. Similarly, positive results have been shown by GALLEFOSS [11] in mild-to-moderate COPD patients after 1-yr follow-up. Two main factors might explain the inconclusive findings on this issue, namely the heterogeneity of the patients examined and the insufficient standardisation of the interventions in these studies.

It can be reasonably assumed that together with the severity of the disease [2], concomitant factors, such as comorbidities, patient's anxiety/depression [14], uncovered social needs and poor self-management of the disease, may modulate hospitalisation rates in these patients. In this scenario, it was hypothesised that a simple, well-defined integrated care (IC) intervention [15, 16], with the support of information and communication technologies (ICT), may be effective to prevent hospitalisations for exacerbations in COPD patients. The novelty of the current study's approach is that the preventive intervention relied on shared-care arrangements between primary care teams and hospital teams, which aimed to avoid duplicates and to generate synergies among different levels of the healthcare system.

The current study was conducted in two cities, Barcelona (Spain) and Leuven (Belgium), with

For editorial comments see page 4.

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marked differences in the primary care settings. Consequently, the intervention required customisation to country specificities, particularly regarding the interactions between hospital and primary care teams. While the general practitioners (GPs) played a key role in Leuven, the intervention in Barcelona was essentially carried out by specialised nurses.

METHODS

Selection and description of participants

The current prospective controlled study was carried out in 155 COPD patients recruited into two tertiary hospitals (Hospital Clínic, Barcelona and University Hospital Gasthuisberg, UZ-Leuven, Leuven) immediately after the patients' hospital discharge. All of the patients were admitted because of a previous episode of exacerbation requiring hospitalisation for >48 h. Up to 850 COPD patients were screened, but only 19% fulfilled the defined criteria and were finally included for randomisation. Exclusion criteria for the study were: 1) not living in the healthcare area (39%); 2) severe comorbid conditions, *i.e.* lung cancer or other advanced malignancies, and extremely severe neurological or cardiovascular disorders (25%); 3) logistical limitations due to extremely poor social conditions, such as illiteracy or no phone access at home (10%); and 4) being admitted to a nursing home (7%). All participants were informed in detail of the characteristics of the study and written informed consent was obtained in accordance with the Committee on Investigations Involving Human Subjects at the two centres, which approved the study. Only five (3%) patients out of 160 did not accept to participate in the study.

All 155 patients (Barcelona n=113, Leuven n=42) included in the study were blindly assigned (1:1 ratio) using computer-generated random numbers to either IC or usual care (UC). As a different randomisation ratio was used in one of the centres (Barcelona 1:2 ratio) during part of the study, the interventions (IC and UC) had different numbers of patients (n=65 and n=90, respectively). The follow-up period was prolonged for 1 yr.

Figure 1 displays a patient's flow throughout the study. The primary end-point was hospital re-admission. In the two centres, re-hospitalisation was assessed through hospital records and systematic questionnaires on use of healthcare resources administered to patients as described in detail below. Mortality and utilisation of healthcare resources were also assessed.

IC intervention

The IC intervention was standardised for both centres, although slightly adapted to the two different healthcare systems and local geographical conditions. It included four key features. First, a comprehensive assessment of the patient at discharge, including severity of the respiratory disease, evaluation of comorbid conditions and analysis of requirements in terms of social support. Secondly, an educational programme on self-management of the disease administered at discharge, as described below. Thirdly, agreement on an individually tailored care plan following international guidelines [2, 17] was shared across the system *via* interaction between the specialised nurse case manager and the primary care team. Fourthly, accessibility of the specialised nurse to

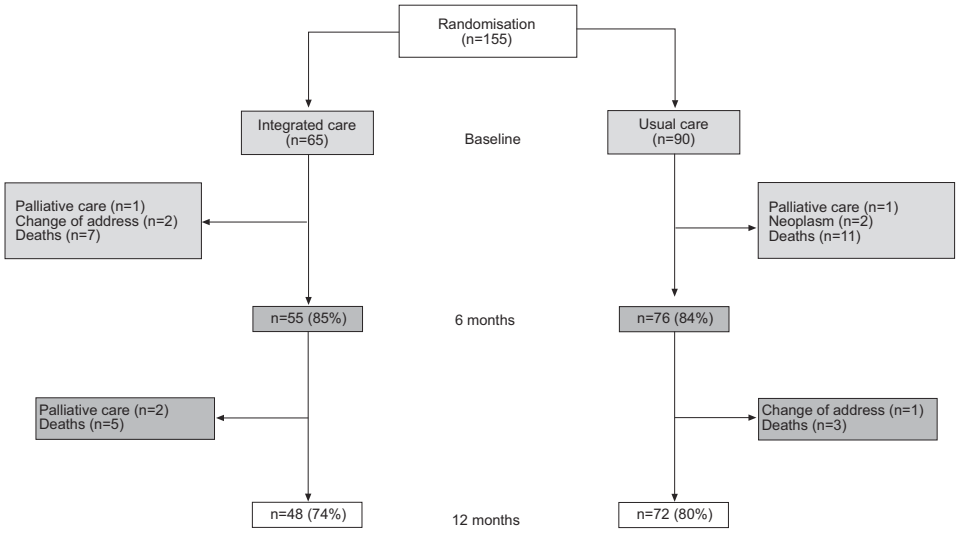

FIGURE 1. Schematic representation of the study profile over 1 yr. In total, 155 chronic obstructive pulmonary disease patients were included in the study. The patients were randomly assigned to integrated care or to usual care. The flow chart shows that all drop-outs during the follow-up were due to either exclusion criteria or death.

patients/carers and primary care professionals during the follow-up period was ensured through an ICT platform including a web-based call centre (CHRONIC project (an Information Capture and Processing Environment for Chronic Patients in the Information Society), IST- 1999/12158).

In both hospitals, all patients in the IC arm of the study (together with their carers, if needed), undertook a comprehensive educational programme of ~2 h duration immediately before discharge, which was administered by a specialised respiratory nurse. This programme covered several items, including knowledge of the disease, instructions on nonpharmacological treatment, assessment of administration techniques for pharmacological therapy and empowerment for self-management of the disease, including strategies to adopt during future exacerbations [15, 17]. In each IC patient, the therapeutic plan was customised to the individual fragility factors [15] described below, and was shared with the primary care team. Reinforcement of the logistics for treatment of comorbidities and social support was carried out accordingly.

A different logistic approach was undertaken in the two study sites due to both geographical factors and specificities of the primary care structure. In Barcelona, one joint visit of the specialised nurse and the primary care team (physician, nurse and social worker) was performed at the patient's home within 72 h of discharge. During the follow-up period, the specialised nurse played the role of case manager.

In Leuven, the GPs planned regular visits to chronic patients, usually at home. The current study aimed at improving these visits regarding COPD care. It is important to realise that each patient in Leuven was allocated to a different primary care physician. GPs were invited to participate in regional education sessions aimed at enhancing knowledge on transmural care for patients with COPD (including information on the current study). Written information brochures on standard treatment plans and treatment guidelines for patients with COPD were sent to the primary care physicians. More importantly, the senior investigator in Leuven (M. Decramer) contacted the individual general practitioner (GP) of patients included in the treatment group. During this contact the treatment plan and points of attention in the healthcare management plan were discussed based on the individual patient files and identified points of fragility.

At both sites, weekly phone calls during the first month after discharge were carried out to reinforce self-management strategies. Phone calls were carried out after 3 and 9 months to inquire about utilisation of healthcare resources with no educational intervention. It is important to note that the IC intervention did not include further scheduled visits by the programme team during the follow-up period in either site. Nonscheduled visits could be triggered by the patients or their carer through the call centre.

The chronic platform

The chronic platform [18] facilitated accessibility of patients/carers and primary care professionals to the specialised nurse case manager. The central component of this ICT platform was a call centre coupled to a web-based application that provided access to and facilitated the management of records of the patients included in the programme. Technical and functional details of the ICT platform are reported elsewhere [18].

UC intervention

Patients included in the UC arm were discharged from hospital by the attending physician who decided on the outpatient control regime. Pharmacological prescriptions at discharge and in-hospital treatment followed the standard protocols of the centres involved in the study, which were similar in IC and UC [2, 17]. Patients in the UC arm of the study were visited by their own physician without additional support. Visits were usually scheduled every 6 months. Specifically, the controls did not receive help from the specialised nurse, nor were they included in the educational programme or had access to the call-centre.

Measurements and instruments

Early assessment of patients at study admission was identical for both groups. Assessment included a blind administration of a questionnaire, described in detail elsewhere [15, 19], concerning: 1) risk factors for exacerbation (vaccination, smoking habits, comorbidities); 2) health-related quality of life status during the previous year (Saint George Respiratory Questionnaire and Euroqol); 3) history of previous exacerbations requiring in-patient hospitalisations and/or emergency room admissions (information was validated by examination of individual clinical records); 4) clinical features of the current exacerbation; 5) fragility factors, such as comorbid conditions, anxiety/depression, educational level, economic status and caregiver support [15]; and 6) treatment, including compliance, observed skills for administration of inhaled drugs, oxygen and physical activity. Vital signs, chest radiography films and pulmonary function tests (including arterial blood gases) were obtained in all patients upon admission.

Assessment of the use of healthcare resources by phone or personal interview was carried out at 1, 3, 6, 9 and 12 months in both arms of the study. Data regarding admissions during follow-up were obtained from hospital records. Data regarding mortality were obtained from hospital records and direct family interviews.

Statistics

Sample size calculation was obtained considering an IC:UC ratio of 1:1.5; thus, estimating a proportion of 60% admitted in the UC group and accepting an alpha risk of 0.05 and a beta risk of 0.20 in a two-sided test. A sample size of 60 IC patients and 90 UC patients was necessary to recognise a statistically significant relative risk of readmission $\geqslant$1.4 in the UC *versus* the IC group. A drop-out rate of 0.15 was anticipated.

Results are expressed as mean$\pm$SD, median (25th percentile–75th percentile), or as percentages in the corresponding categories. Comparisons between UC and IC on admission were performed using independent unpaired t-tests, a non-parametric Mann–Whitney U-test or the Chi-squared test. All analyses were conducted according to the intention-to-treat principle. Sequential survival analysis was performed with a Cox proportional-hazards model to determine whether IC assignment was an independent predictor of hospitalisation after adjustment for variables that were different at baseline, *i.e.* hospital respiratory admissions in the previous year and

influenza vaccination. Data regarding patients who died without re-admission were censored at the time of death. All analyses were carried out separately in each centre and also with pooled data. The use of healthcare resources was expressed as rate of re-admissions calculated as the number of re-admissions during the follow-up times (number of follow-up days/365). The difference in rate of re-admissions per year is expressed as the number of re-admissions during the follow-up year minus the number of re-admissions in the previous year. Survival without re-admission corresponds to subjects with no re-admissions among survivors. Differences between IC and UC were examined using the Kruskal–Wallis tests. Statistical significance was accepted at $p<0.05$.

RESULTS

A total of 155 COPD patients who were discharged from two tertiary hospitals (Barcelona and Leuven; fig.1) were included in the analysis (IC=65 and UC=90). Drop-outs for the entire follow-up period are described in figure 1. As indicated in table 1, at entry, the patients of the two interventions showed similar characteristics except for the number of hospital admissions in the previous year (1.0±1.3 *versus* 0.64±1.2 in the IC and UC group, respectively; p=0.05) and influenza vaccination (56 *versus* 78%, respectively; p=0.01).

Since only patients with COPD and lack of very severe comorbidities or extreme social problems were considered eligible for the current study, the current authors compared relevant variables between participants and subjects excluded from the current study. The analysis showed that subjects excluded from the study had more chance of being female (p=0.011) and older (mean difference 2 yrs; p=0.02), and less chance of being smokers (p=0.002) than the participants. No differences in the remaining variables, including intensive care unit admissions, were observed.

Main outcomes

IC was associated with a lower re-hospitalisation rate during follow-up than UC. The hazard ratio (HR) estimated by adjusted Cox analysis was 0.55 (95% confidence interval (CI) 0.35–0.88; p=0.01) for Barcelona and Leuven as analysed jointly (fig. 2). The figure also displays a separate analysis of the two sites, showing similar results between Barcelona (HR 0.52 (95% CI 0.28–0.95); p=0.04) and Leuven (HR 0.35 (95% CI 0.15–0.80); p=0.01).

The main outcome variables of the analysis with pooled data are displayed in table 2, indicating that IC clearly presented a lower number of re-hospitalisations than UC (p=0.02). The remaining variables in the table further support the contention that IC prevented hospitalisations compared with UC. The rate of readmissions (1.5 *versus* 2.1, p=0.033) were significantly lower in the IC intervention than in UC. Likewise, the percentage of patients without admissions among survivors was also greater in IC (49%) than in UC (31%; p=0.03). No significant differences regarding deaths were observed in IC and UC, 19 and 16%, respectively.

The difference in rate of admissions per patient between the follow-up and the previous year was also lower in IC (0.47±2.4) than in UC (1.84±3.95; p=0.03).

TABLE 1 Baseline characteristics

	IC	UC	p-values
Subjects	65	90	
Sociodemographics			
Age yrs	70±9	72±9	0.09
Sex (females)	15 (23)	11 (12)	0.64
Education less than primary	16 (25)	20 (22)	0.85
Annual income <€6000	7 (13)	16 (24)	0.16
Clinical and functional profile			
Length baseline hospitalisation	8.5±5.5	7.8±4.2	0.65
MRC dyspnoea scale	3.5±1.3	3.5±1.2	0.84
BMI kg·m^{-2}	26.4±5.1	26.1±5.4	0.71
FVC % pred	64±21	63±18	0.79
FEV_1 % pred	43±20	41±15	0.89
FEV_1/FVC %	48±18	48±17	0.95
P_{a,O_2} mmHg	64±11	64±14	0.65
P_{a,CO_2} mmHg	44±7	44±7	0.87
Comorbidities	1.9±1.4	1.8±1.5	0.74
Hospital respiratory admissions previous yr	1.0±1.3	0.6±1.2	0.05
SGRQ total score	57±18	59±18	0.46
Euroqol analogue visual scale#	47.8±18.1	47.4±18.5	0.87
Anxiety and depression Goldberg score	8.5±5.6	8.2±5.9	0.71
Apgar score¶	7.6±4.2	6.3±2.9	0.18
Regular COPD treatment			
LTOT	16 (25)	21 (23)	0.85
Influenza vaccination	36 (56)	68 (78)	0.01
Pneumococcal vaccination	19 (36)	41 (53)	0.07
Home rehabilitation	17 (26)	20 (22)	0.57
Self-management			
Active smokers	21 (32)	19 (21)	0.14
Knowledge-name and cause of the disease	45 (69)	58 (65)	0.61
Poor adherence to inhalers	14 (23)	23 (28)	0.56
Regular physical activity	56 (86)	82 (91)	0.43
Knowledge alarm symptoms and drugs	44 (68)	66 (73)	0.48

Data are presented as n, mean±SD or n (%). IC: integrated care; UC: usual care; MRC: Medical Research Council scale for scoring dyspnoea; BMI; body mass index; FVC: forced vital capacity; % pred: % predicted; FEV_1: forced expiratory volume in one second; FEV_1/FVC ratio: expressed as actual value; P_{a,O_2}: arterial oxygen tension; P_{a,CO_2}: carbon dioxide arterial tension; SGRQ: Saint George's Respiratory Questionnaire to assess health-related quality of life; Apgar: adaptability, partnership, growth, affection and resolve; COPD: chronic obstructive pulmonary disease; LTOT: long-term oxygen therapy. #: instrument to assess health-related quality of life; ¶: to assess family functionality. 1 mmHg=0.133 kPa.

Use of healthcare resources

Table 3 displays the main data on utilisation of both scheduled and nonscheduled services in the two sites. No significant differences were observed between IC and UC in the number of visits. It is of note that all results in table 3 are expressed as median (25th percentile–75th percentile). In Barcelona (IC=44), a total of 448 phone calls through the call centre, 194 (43%) scheduled and 254 unscheduled, were carried out during the 12-month follow-up period. In Leuven (IC=21), the total number of phone calls during the study was 201, 128 (63%)

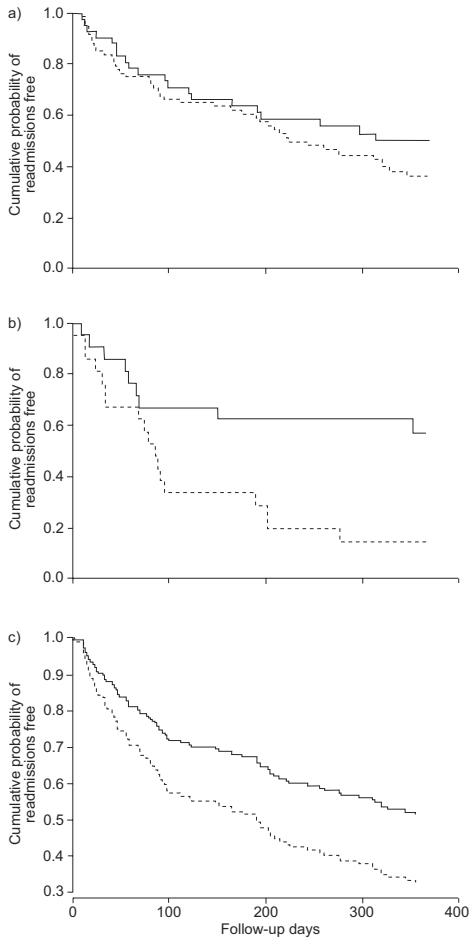

FIGURE 2. The results of the Cox analyses carried out separately in a) Barcelona and b) Leuven. c) The results of the analysis carried out with pooled data in both centres. In all cases, chronic obstructive pulmonary disease patients in integrated care (—) showed a higher rate of admission-free time than usual care (- - -). a) Hazard ratio (HR) 0.52 (95% confidence interval (CI) 0.28–0.97), p=0.04; b) HR 0.35 (95% CI 0.15–0.80), p=0.01; c) HR 0.55 (95% CI 0.34–0.87), p=0.01.

scheduled and 73 unscheduled. In this centre, only five (22%) out of the 22 patients used the service by triggering the phone call. Fourteen (67%) out of the 21 patients in the IC intervention received unscheduled phone calls by the specialised nurse. Unscheduled phone calls were mostly related to worsening of symptoms (patient-triggered) or follow-up of exacerbations (nurse-triggered). The mean duration of the phone calls in the two sites was ~20 min. In Leuven, no home visits by hospital-based specialised nurses were planned after discharge.

TABLE 2 Main outcomes

	IC	UC	p-value
Subjects	65	90	
Number of readmissions			
0	36 (55)	30 (33)	0.028
1	14 (22)	34 (38)	
⩾2	15 (23)	26 (29)	
Number of readmissions during follow-up year	0.9±1.3	1.3±1.7	0.028
Rate of readmissions during follow-up year	1.5±2.6	2.1±3.1	0.033
Difference on rate of re-admissions per year	0.5±2.6	1.5±3.1	0.003
Survival without readmissions	32 (49)	28 (31)	0.03
Total deaths	12 (19)	14 (16)	0.67

Data are presented as n, n (%) or mean±SD. IC: integrated care; UC: usual care. Rate of re-admissions during the follow-up year was calculated as the number of re-admissions during the follow-up × number of follow-up days/365. The difference in rate of re-admissions per year is expressed as the number of re-admissions during the follow-up year minus the number of re-admissions in the previous year. Survival without re-admission corresponds to subjects with no re-admission among survivors.

DISCUSSION

The present study demonstrates the effectiveness of a well-defined low-intensity IC programme in COPD patients to prevent future exacerbation episodes triggering hospital admissions. In the current study, three major novel aspects were identified: 1) standardisation of the IC intervention; 2) pilot development of a distributed model with shared arrangements between primary care, hospital and community services; and 3) use of ICT as a supporting tool for the programme. It must be highlighted that the effects of the IC intervention were similar in both countries. The intervention was customised to the organisational specificities of primary care in the two participating countries, but its most distinctive feature was common in both sites, that is, to promote standardised shared-care arrangements between levels of care to prevent COPD exacerbations.

In the current study, as opposed to previous reports on prevention of hospitalisations for exacerbations in COPD patients [10, 12], the educational programme was only one of the components of the IC strategy. The effectiveness of IC can be explained by different concomitant factors. It can be reasonably assumed that the intervention resulted in enhanced self-management of the disease together with a higher accessibility to healthcare professionals. Likewise, the potential impact of the intervention on enhanced management of comorbid conditions and social problems cannot be neglected. Altogether the interventional impact may have prompted an early detection and better management of exacerbations in the IC programme. A recent report by WILKINSON *et al.* [20]

indicates that patient recognition of exacerbation symptoms and prompt treatment in COPD patients improves exacerbation recovery and reduces risk of hospitalisation. It is also associated with a better health-related quality of life.

Preliminary analyses of other follow-up variables in a subsample of these patients, not reported in the current study, showed no differences in smoking habits or physical activity practice at 12 months between UC and IC. However, it is of note that all variables related to COPD knowledge, self-management and adherence to treatment were better scored in IC than in UC. No differences between groups were found in pharmacological therapies, physical rehabilitation or in patient satisfaction.

Internal and external validity of the trial

Adequacy of the assignment process to either IC or UC was ensured by both the generation of the allocation sequence by a random process and preventing foreknowledge of the treatment assignments in the specialised team that implemented the allocation sequence. As described previously, the different randomisation ratio in the two centres provoked an imbalance in the number of patients assigned to each arm of the study (IC=65 and UC=90). The ratio 1:2 was transiently used in the Hospital Clínic (Barcelona) as a conservative approach to ensure appropriate logistics for the study. The allocation sequence alluded to above cannot explain the differences between IC and UC at entry of the study (table 1) observed in Barcelona. As indicated previously, the statistical analysis included adjustment for variables which were different at baseline (number of hospital admissions in the previous year and influenza vaccination). Moreover, the consistency of the results in Barcelona was further ensured by examining the history of hospitalisations in the previous 2 yrs for both IC and UC. A strength of the present analysis was that there were no subjects lost to follow-up, since all drop-outs were due to appearance of exclusion criteria or death (fig. 1) and, in any case, valid information about re-hospitalisations was available from the national health services.

Despite the IC intervention being adapted to the specificities of the healthcare system in each site, it showed, as a common and most distinctive feature, the development of planned shared-care arrangements between levels of care. In Barcelona specifically, one joint visit of the specialised nurse and the primary care team at the patient's home was carried out within 72 h of discharge. This approach was chosen because of its practicality, as the hospital is the reference centre of a geographically small, but highly populated (500,000 inhabitants) urban sector. In contrast, the UZ-Leuven centre covers a large geographical area and patients live in remote areas away from the hospital, making the initial joint visit to the patient's home impractical. In addition, GPs in Belgium are stimulated to play a role as ''gate keepers'' of the healthcare system.

The initial joint visit in Barcelona was likely to be useful for implementation of individualised care plans shared by patients/care givers, primary care professionals and the hospital team. In Leuven, the beneficial effects of the intervention should also be attributed to the planned shared care arrangements between hospital-based professionals and primary care doctors, as described above. Since the Leuven site did not show statistical significant differences in the number of GP visits (table 3), it is reasonable to assume that the intervention enhanced the quality of these visits, leading to improved clinical outcomes as seen in the IC group (fig. 2). In other words, the beneficial effects of the IC intervention did not seem to be associated with the number of home visits carried out either by a nurse (Barcelona) or a primary care physician (Leuven).

TABLE 3 Use of healthcare resources[#] (rate per year) during the follow-up

	IC	UC	p-value
Subjects	65	90	
Follow-up time days[¶]			
Barcelona	297±115	319±100	0.088
Leuven	365	365	
Nurse home visits within the programme			
Barcelona	3 (1–10)		
Leuven	NP		
Doctor visits			
Barcelona[+]	2 (0–4)	2 (1–4)	0.437
Leuven GPs at home	10 (7–18)	13 (9–27)	0.454
Phone calls patient-triggered			
Barcelona	2 (0–8)		
Leuven	0 (0–0)		
Phone calls follow-up intervention			
Barcelona	1 (1–3)		
Leuven	2 (0–3)		

Data are presented as n, mean±SD or median (25th percentile–75th percentile). IC: integrated care; UC: usual care; NP: not planned; GP: general practitioner. [#]: expressed as the number of visits per patient and follow-up time; [¶]: all subjects were included until the last day of follow-up or date of exclusion, whichever was first; [+]: includes unplanned visits to the GP, specialist outside the hospital, pneumologist from the hospital, private doctors, domiciliary visits from the primary care team and visits to the day hospital.

In the current study, the outcomes of the IC intervention after stratification by disease severity were not reported. The latter should be addressed considering different covariates, namely Global Initiative for Chronic Obstructive Lung Disease classification [2], history of previous exacerbations and comorbid conditions not leading to exclusion criteria. This assessment was not done partly because of insufficient statistical power of the study for this specific purpose. However, it is of note that the current disease-orientated programme only allowed inclusion of 155 COPD patients. This figure represents 452 (34%) of all screened COPD patients living in the healthcare sector and willing to participate in the study. It can be reasonably assumed that no selection bias was present due to exclusion of those patients not living in the healthcare sector (n=331). A rough revision of the current underlying reasons for exclusion indicates that most of the 452 COPD patients would have been eligible for properly tailored patient-centred IC programmes. It can be argued that a patient-focused strategy instead of the current disease-orientated approach must be adopted to properly fulfil the principal aims of the Chronic Care Model [21, 22]. In the present study,

an IC pathway for COPD has been successfully applied, but from the screening data it has become clear that patients with cancer, severe neurological or cardiovascular disorders (n=212), or those who were indigent (n=145) required a specific integrated pathway either across several medical specialities and/or appropriate social support, respectively. The approach adopted in the current study may limit its external validity, as in most clinical trials by definition, but increases internal validity. Given the very small number of nonresponses (five subjects, 3% of the eligible), the current authors' opinion is that eligibility criteria, although restrictive, allow for a highly valid estimation of the effect of an IC programme in COPD patients without severe comorbidities. In other words, the study design reinforces the present author's conclusion on the beneficial effects of IC to prevent hospitalisations in the COPD patients studied, but the results cannot be generalised to all elderly COPD patients with very severe comorbid conditions admitted to the emergency room because of an episode of exacerbation.

Analysis of the economical implications of the intervention was beyond the scope of the present study. However, it is of note that the outpatient consultations outside of the IC programme were similar between both arms of the study. Likewise, the number of home visits in the IC group and the requested activity through the call centre during the 12-month follow-up were rather modest. The total number of phone calls per patient through the call centre was similar in both countries. However, only a small percentage of patients in Leuven (24%) triggered phone calls, which was not the case in Barcelona. This phenomenon had no implication on outcomes and it can be explained by differences in primary care between Belgium and Spain. Overall, the present authors understand that the extension of the IC intervention has a clear potential for cost-containment because of the significant savings generated in both direct and indirect costs due to prevention of hospitalisations. Moreover, the homogeneity of the outcomes in the two sites, together with the simplicity of the intervention, indicates that the proposed strategy shows potential for a successful deployment in other healthcare systems.

IC and information technologies

The conceptual aspects of planned care for chronic patients were originally formulated by WAGNER [21] and were subsequently adopted by the World Health Organization [22]. Encouragement of preventive strategies promoting behavioural changes in life style and the design of innovative home-based services must become components of integrated care strategies within regional networks, by no means confronted to patient hospitalisation. In building up such strategies, the establishment of effective functional relationships among levels of care will preclude the current fragmentation of services. Activities included in the integrated interventions explored in the current study cannot easily be made operative in the absence of a robust ICT support.

In conclusion, the integrated care intervention proposed in the current study significantly improved the management of moderate-to-severe chronic obstructive pulmonary disease patients and facilitated the logistics for an appropriate long-term follow-up of these patients. The current authors understand that the prevention strategy examined in the present study constitutes a valid contribution to be considered in future versions of the chronic obstructive pulmonary disease guidelines [2, 17].

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Manuscrito 5

Effects of an integrated care intervention on risk factors of COPD readmission
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Effects of an integrated care intervention on risk factors of COPD readmission

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KEYWORDS
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Summary
An integrated care intervention including education, coordination among levels of care, and improved accessibility, reduced hospital readmissions in chronic obstructive pulmonary disease (COPD) after 1 year. This study analyses the effectiveness of this intervention in terms of clinical and functional status, quality of life, lifestyle, and self-management, under the hypothesis that changes in these factors could explain the observed reduction in readmissions.
A total of 113 exacerbated COPD patients (14% female, mean (SD) age 73(8) years, FEV_1 1.2(0.5) l) were recruited after hospital discharge in Barcelona, Spain, and randomly assigned (1:2) to integrated care (IC) ($n = 44$) or usual care (UC) ($n = 69$). The intervention consisted of an individually tailored care plan at discharge shared with the primary care team and access to a specialized case manager nurse through a web-based call centre.
After 1 year of intervention, subjects in the intervention group improved body mass index by 1.34 kg/m^2. Additionally, they scored better in self-management items: COPD knowledge 81% vs. 44%, exacerbation identification 85% vs. 22%, exacerbation early treatment 90% vs. 66%, inhaler adherence 71 vs. 37%, and inhaler correctness 86 vs. 24%. There were no differences in the evolution of dyspnea, lung function, quality of life scores, lifestyle factors, or medical treatment.
Conclusions: This IC trial improved disease knowledge, and treatment adherence, after 1 year of intervention, suggesting that these factors may play a role in the prevention of severe COPD exacerbations triggering hospital admissions.

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Introduction

The burden of chronic obstructive pulmonary disease (COPD) is very high in terms of prevalence, morbidity, mortality and economic costs.[1] The need to reduce this burden, in the context of a general concern about chronic diseases management,[2] has prompted the development of new management strategies for COPD. These strategies focus particularly on the active role of the individual[3] (self-management programmes), with the aim of avoiding the rigidity and fragmentation of traditional healthcare systems.[4,5] The intervention relies on care arrangements being shared between professionals working in different levels of the healthcare system and promotes accessibility of target patients to healthcare professionals following well-standardized procedures.[6] Knowledge about effectiveness and cost of these new approaches in COPD is still scarce.

Self-management education programmes try to teach patients how to carry out the activities of daily living optimally, and to prevent or decrease the severity of exacerbations by early recognition and treatment of the episodes.[7] A self-management programme in COPD patients in Quebec reduced hospital admissions and emergency-room visits during the 1 year study period.[8] Patients maintained a significant reduction in hospitalization risk after a 2-year period.[9] However, most of the educational programmes have found negative or inconclusive results with regard to health services use, lung function, respiratory symptoms or health-related quality of life.[7] An innovative management strategy is hospital at home or supported discharge, which are proposed as an alternative to hospital admission when a COPD exacerbation appears, to increase patients' satisfaction and reduce costs, without adverse health effects for the patients.[10] Compared to inpatient treatment, hospital at home or supported discharge programmes reduce costs, free up hospital inpatient beds, and are safe for the patients, but do not change risk of hospital readmission or mortality.[10] Recently, systematic reviews of educational and home hospitalization programmes have revealed that differences in populations under study, in content of the programmes, and in outcome measures, make the generalization of their results difficult, implying that more research is needed in this area before recommending these treatments.[7,10]

In a recent paper, we reported that an integrated care intervention including education, coordination among levels of care, and improved accessibility, reduced hospital readmissions in COPD after 1 year of follow-up by 50%, in a randomized controlled trial in 155 COPD patients from Barcelona, Spain, and Leuven, Belgium, both in the pooled and by-site analysis.[6] The present analysis in the subgroup of patients from Barcelona, aims to assess the effectiveness of this intervention in terms of enhancing clinical status (dyspnea, body mass index (BMI)), health-related quality of life, lifestyle (smoking, physical activity), self-management (COPD knowledge, alarm knowledge and treatment, treatment adherence), medical treatment, and patients' satisfaction, after a 1-year follow-up period, under the hypothesis that changes in these factors could explain the reduction in readmissions. Functional status (lung function and arterial blood gases) was also measured.

Methods

Design

Randomized controlled trial, subjects were assessed at baseline. The follow-up period was prolonged for one full year with patient's assessment performed at 6 and 12 months.

Subjects

A total of 113 COPD patients were consecutively recruited during 1 year in one tertiary hospital (Hospital Clínic) in Barcelona, Spain, immediately after hospital discharge, and were blindly assigned (1:2 ratio) using computer generated random numbers either to integrated care (IC) or to usual care (UC). All of them had been admitted because of an episode of exacerbation requiring hospitalization for more than 48 h. Exclusion criteria for the study were: (1) not living in the healthcare area or living in a nursing home; (2) lung cancer or other advanced malignancies; (3) logistic limitations due to extremely poor social conditions, illiteracy, or no phone access at home; and (4) extremely severe neurological or cardiovascular co-morbidities. All participants were informed in detail of the characteristics of the study, and written informed consent was obtained in accordance with the Committee on Investigations Involving Human Subjects at the hospital.

Integrated care (IC) intervention

The IC intervention has been described in detail elsewhere[6] and includes 4 key features. First, a comprehensive assessment of the patient at discharge including severity of the respiratory disease, evaluation of co-morbid conditions, treatment adherence, and analysis of requirements in terms of social support, was done by a specialized nurse. Secondly, an educational session of approximately 2 h duration on self-management of the disease was administered at discharge, also by the specialized respiratory nurse specifically trained for the study intervention. This session covered several items, including knowledge of the disease, smoking cessation, promotion of physical activity, nutrition recommendations and other instructions on non-pharmacological treatment, assessment of correctness of administration techniques for pharmacological therapy and teaching of self-management strategies to cope with future exacerbations.[11,12] Written information was provided to all patients.[13] Education on skills to identify clinical deterioration was an important aspect of the programme. Patients were taught to generate a phone call to the call centre if symptoms or signs indicating clinical deterioration occurred. The call was transferred to a specialized nurse (case manager) that either solved the problem by phone or triggered a home visit. Thirdly, an individually tailored care plan, following international guidelines,[12,14] was elaborated through the interaction between the specialized nurse case manager and the primary care team. Reinforcement of the logistics for treatment of co-morbidities and social support was done accordingly. One joint visit of the specialized nurse and the primary care team (physician, nurse and social

worker) to the patient's home was made within 72 h after discharge. Weekly phone calls during the first month after discharge and one phone call at months 3 and 9 were carried out to reinforce self-management strategies. Lastly, access to the specialized nurse at the hospital was guaranteed to patients, caregivers and primary care professionals during the follow-up period through an Information and Communication Technologies (ICT) platform including a web-based call centre.[15] It is important to note that the IC intervention did not include further scheduled visits during the follow-up period. Non-scheduled visits could be triggered by the patients through the call centre.

Usual care (UC) group

Patients included in the UC group were discharged from the hospital by the attending physician who decided on the outpatient control regime. Pharmacological prescriptions at discharge and in-hospital treatment followed the standard protocols of the centre and were similar in the two groups (IC and UC).[12,14] However, patients did not receive the support of a specialized nurse which included the educational session, joint visit with the primary care team, nor was access to the call-centre provided.

Variables and instruments

Early assessment of patients at their admission to the study was identical for both groups. It included a blind administration of a questionnaire, described in detail elsewhere[11,16] concerning: sociodemographic factors (sex, age, educational level, economic status and caregiver support); clinical factors (co-morbidities, dyspnea (Medical Research Council scale), body mass index (BMI), and previous hospital and emergency room admissions due to COPD); health-related quality of life (Saint-George's Respiratory Questionnaire (SGRQ) and Euroqol (EQ-5D)); lifestyle (smoking, alcohol, and physical activity); self-management (knowledge about symptoms and treatment of COPD, identification and early treatment of a COPD exacerbation, treatment adherence—using the Medication Adherence Scale (MAS) and Inhaler Adherence Scale (IAS),[17] and observed skills for administration of inhaled drugs[18]); drug (short and long-acting β_2-agonists, anticholinergics, methilxanthines, inhaled and oral corticosteroids) and non-drug treatment (vaccines, oxygen therapy); and satisfaction with health services. Vital signs, chest X-ray films, and pulmonary function tests, including arterial blood gases, were obtained in all patients on admission.

At 6 and 12 months of follow-up, the same questionnaires and lung function tests were administered to the two arms of the study together with a detailed list of questions on the utilization of healthcare resources during each period.

Statistical analysis

Results are expressed as mean (SD), median (P_{25}–P_{75}), or as number (percentage) in the corresponding categories. To assess the possibility of selection bias, comparisons of baseline characteristics between UC and IC, both for the followed-up and for the lost subjects were performed using independent *t*-tests, Kruskal–Wallis test or the Chi-square test, depending on the distribution of each variable. Since data about outcome variables was not available in the lost subjects (whether due to exclusion, loss to follow-up or death), an intention-to-treat principle was not possible. Thus, all analyses about the impact of intervention were restricted to subjects with complete data during the follow-up. No values were imputed to subjects lost to follow-up. Four approaches were used. First, for continuous variables, the difference between 12 months values and baseline values was modelled using linear regression. Second, for categorical variables, the difference between 12 months and baseline values was turned into three categories (no change, improvement, or impairment), which were modelled using politomic logistic regression. Since many of the variables had a very small number of subjects in some categories, the politomic logistic regression led to large confidence intervals. Therefore, and considering that there were no baseline differences in these categorical variables between the UC and IC groups, final (12 months) values were directly compared between groups using chi-square test, and these are the results which are actually shown. Finally, variance analysis with repeated events, which allowed to include 6 months values and a better modelling of changes over time, was also used for all outcome variables. This analysis provided both differences among groups (*p*-group effect) and differences among periods (*p*-time effect). No adjustment for baseline variables was done in any of the approaches, since there were no baseline differences between groups.

Results

Fig. 1 displays patient's flow throughout the study. One hundred and thirteen subjects were identified and randomly assigned to the intervention or control group. Five subjects refused to participate. During follow-up, *a priori* defined exclusion criteria, such as lung cancer, appeared in 9 subjects. Twenty-one subjects died, and 16 were lost to follow-up. Only 57% of subjects finished the study at 12 months.

Subjects were mostly male, over 70 years old, and suffered from severe COPD. Table 1 shows baseline characteristics of the subjects, comparing the UC and IC groups, according to whether subjects were lost or completed the follow-up. No differences were found at baseline between the UC and IC groups, except for the SGRQ score, which was lower in the IC group than the UC group among those that completed the follow-up, this difference being clinically important although not statistically significant. No differences in adherence, drug and non-drug treatments were found (not shown). Subjects who were lost for the present analysis had a higher number of COPD admissions in the previous year and in the follow-up year, and they were using long-term oxygen therapy in a higher proportion than those subjects who participated in the 12 months assessment.

Table 2 shows changes (difference between 12 months and baseline) in clinical, functional and quality of life variables, by groups of treatment, as well as the difference of this change in the IC group compared to the UC group, which is equal to the coefficient of the linear regression model. Dyspnea worsened slightly in both groups during the follow-up period. Body mass index did not change in the UC

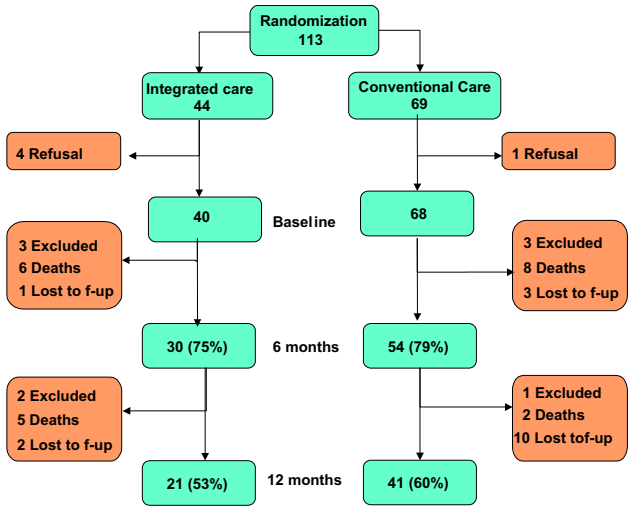

Figure 1 Flow chart of patients participation in the study.

group while it increased in the IC group, this difference being statistically significant. Lung function did not change in any group. Arterial oxygenation improved in both groups, without statistically significant differences between groups. Quality of life scores (according to the SGRQ and the Euroqol visual analogue scale) slightly improved in the follow-up year, without differences between groups, with the exception of the symptoms score, which improved more in the IC group, this difference not being statistically significant.

There were no differences in smoking habits or physical activity practice at 12 months between the UC and IC groups (Table 3). All variables related to self-management (COPD knowledge, identification and treatment of a COPD exacerbation, and adherence to treatment), were better in the IC group than in the UC group, most of these differences being statistically significant. There were no differences in pharmacological or non-pharmacological treatments, or degree of satisfaction of the patients between groups.

Variance analysis with repeated events, which allowed inclusion of 6 months values, was performed for all variables. With the exception of PaO_2, no additional information was obtained from this analysis, since most variables followed the same pattern in the various intervals (baseline—6 months, 6–12 months, baseline—12 m). However, PaO_2 improved between baseline and 6 months in both groups, and afterwards improved further in the IC group while it worsened in the UC group (Fig. 2).

Discussion

This is one of the few studies that have examined and showed that IC, including self-management education, coordination among levels of care, and increased accessibility in COPD patients, is associated with an improvement in disease knowledge, treatment adherence and nutritional status. The study was not able to show changes in lifestyle variables, medical treatment, lung function or quality of life. A complete interpretation of these results needs to consider that this intervention was effective to reduce COPD admission risk.[6]

The intervention improved disease knowledge, consistently with previous trials of self-management,[19] home based care,[20] or respiratory rehabilitation[21]), which included education as a component. The importance of the present findings lies in three key issues: (i) the present programme was not intensive in education, including only a session of 2 h at baseline supported by the practice team; (ii) effects persisted after 12 months, while previous studies, with more intensive interventions, reported effects after shorter periods of follow-up[19,20]; (iii) we also assessed the effect of intervention on hospital admissions, which allows us to hypothesize that the increase in knowledge could be partially responsible for the previously reported reduction in admissions.[6] It is likely that, even without changes in the frequency or severity of COPD exacerbations, subjects with better knowledge and skills may not need hospital admission because of an early treatment of the exacerbation. This is supported by a previous study in a panel of COPD patients which found that early treatment of COPD exacerbation improved exacerbation recovery and reduced risk of hospitalization[22]).

Self-reported adherence to inhaled medication and performance of the inhaler manoeuvre improved in the IC group, according to a previous educational programme which found an improvement in the inhalation technique

Table 1 Subjects' characteristics in usual care (UC) and integrated care (IC) groups, according to follow-up status.

	Lost to follow-up (death, lost or excluded)			Followed-up			*P* (lost vs. followed)
	Usual care (UC) $n = 28$	Integrated care (IC) $n = 23$	*P*	Usual care (UC) $n = 41$	Integrated care (IC) $n = 21$	*P*	
Sex: female *n* (%)	1 (4)	7 (30)	0.009	4 (10)	4 (20)	0.302	0.673
Age (years) *m* (SD)	74 (8)	73 (6)	0.717	73 (9)	72 (10)	0.829	0.675
Less than primary education *n* (%)	5 (19)	8 (36)	0.159	13 (33)	5 (24)	0.480	0.730
Smoking							
Current *n* (%)	3 (11)	4 (17)	0.571	6 (15)	5 (24)	0.571	0.819
Former *n* (%)	23 (82)	16 (70)		31 (76)	15 (71)		
Never *n* (%)	2 (7)	3 (13)		4 (10)	1 (5)		
Dyspnea (MRC scale) Median (P_{25}–P_{75})	4 (3–5)	5 (3–5)	0.197	4 (3–5)	3 (3–4)	0.601	0.390
BMI (kg/m^2) *m* (SD)	25.6 (5.9)	26.3 (5.9)	0.700	27.4 (5.7)	28.1 (4.3)	0.632	0.117
FEV_1 (l) Median (P_{25}–P_{75})	1.1 (0.8–1.5)	1.0 (0.8–1.5)	0.550	1.0 (0.8–1.5)	1.2 (0.8–1.4)	0.512	0.929
FEV_1/FVC (%) *m* (SD)	54 (18)	57 (18)	0.524	51 (18)	48 (17)	0.613	0.126
PaO_2 (mmHg) *m* (SD)	65 (14)	62 (14)	0.399	61 (9)	64 (10)	0.323	0.446
$PaCO_2$ (mmHg) *m* (SD)	43.3 (9.1)	44.1 (8.4)	0.750	43.8 (6.5)	43.1 (6.6)	0.715	0.916
Any comorbidity *n* (%)	27 (96)	19 (83)	0.099	39 (93)	17 (81)	0.167	0.799
COPD admissions in the last year Median (P_{25}–P_{75})	0 (0–1)	1 (1–2)	0.004	0 (0–1)	0 (0–1)	0.929	0.003
COPD admissions during follow-up Median (P_{25}–P_{75})	1 (0–2)	1 (0–2)	0.813	1 (0–1)	0 (0–1)	0.083	0.077
Long-term oxygen therapy *n* (%)	11 (39)	9 (39)	0.991	8 (20)	6 (29)	0.419	0.055
Health-related quality of life (SGRQ)* *m* (SD)	53.4 (19.3)	61.8 (17.6)	0.131	60.5 (20.2)	51.2 (16.9)	0.077	0.951

*Saint-George's Respiratory Questionnaire (SGRQ) score goes from 0 (better health status) to100 (worse health status).

Table 2 Changes in clinical status, functional status, and quality of life between baseline and 12 months, in UC and IC groups (linear regression).

	Change, m (SD) (12 months—baseline values)		Linear regression	
	Usual care (UC) $n = 41$	Integrated care (IC) $n = 21$	coefficient (95% CI)*	*P*
Dyspnea score (MRC)	−0.15 (1.44)	−0.52 (1.12)	−0.38 (−1.1 to 0.34)	0.299
BMI (kg/m^2)	−0.01 (1.63)	1.33 (1.73)	1.34 (0.31 to 2.37)	0.012
FEV_1 (l)	0.06 (0.35)	0.01 (0.14)	−0.05 (−0.24 to 0.14)	0.569
FEV_1/FVC (%)	−1.66 (17.94)	−0.82 (8.18)	0.84 (−8.27 to 10.66)	0.863
PaO_2 (mmHg)	3.12 (8.5)	5.36 (8.54)	2.24 (−2.57 to 7.06)	0.355
$PaCO_2$ (mmHg)	−1.1 (5.57)	−0.26 (5.24)	0.84 (−2.25 to 3.93)	0.588
Specific health-related quality of life (SGRQ†)				
Symptoms	−17.11 (24.44)	−24.4 (19.68)	−7.29 (−19.66 to 5.07)	0.243
Activity	−8.36 (19.95)	−5.08 (16.61)	3.27 (−6.91 to 13.46)	0.523
Impact	−11.29 (16.34)	−13.7 (15.62)	−2.41 (−11.24 to 6.42)	0.587
Total	−11.02 (15.57)	−13.41 (13.43)	−2.39 (−10.56 to 5.78)	0.560
Generic health-related quality of life (Euroqol‡)	0.93 (2.11)	1.56 (1.77)	0.62 (−0.51 to 1.75)	0.273

*Relative change in IC group compared to UC group.
†SRGQ score goes from 0 (better health status) to100 (worse health status). Negative change means improvement.
‡Euroqol score goes from 0 (worse health status) to 10 (better health status). Positive change means improvement.

Table 3 Lifestyle factors, self-management, medical treatment, and health care satisfaction, at 12 months, in UC and IC groups.

	Usual care (UC) $n = 41$	Integrated care (IC) $n = 21$	*P*
No current smokers *n* (%)	36 (88)	20 (95)	0.349
Any physical activity *n* (%)	34 (83)	18 (86)	0.778
Regular walking or exercising *n* (%)	32 (78)	18 (86)	0.470
Knowledge about			
Name of the disease (COPD) *n* (%)	18 (44)	17 (81)	0.005
Identification of a COPD exacerbation *n* (%)	9 (22)	17 (85)	<0.001
Early treatment of a COPD exacerbation *n* (%)	27 (66)	19 (90)	0.036
Adherence to oral treatment (MAS scale)* *n* (%)	35 (85)	19 (90)	0.570
Adherence to inhaled treatment (IAS scale)* *n* (%)	15 (37)	15 (71)	0.009
Correct inhaler manoeuvre *n* (%)	9 (24)	18 (86)	<0.001
Long-term oxygen therapy ⩾16 h *n* (%) $n = 23$	15 (94)	7 (100)	0.499
Influenza vaccination *n* (%)	32 (78)	19 (90)	0.442
Pneumococcal vaccination *n* (%)	25 (61)	16 (76)	0.348
Long-term oxygen therapy *n* (%) *n* (%)	16 (39)	7 (33)	0.661
Short-acting β_2-agonists *n* (%)	36 (88)	21 (100)	0.095
Long-acting β_2-agonists *n* (%)	31 (76)	11 (52)	0.064
Anticholinergics *n* (%)	32 (78)	15 (71)	0.565
Methilxanthines *n* (%)	1 (2)	0 (0)	0.471
Inhaled corticosteroids *n* (%)	30 (73)	19 (90)	0.113
Oral corticosteroids *n* (%)	1 (2)	2 (10)	0.219
Satisfaction with health care *n* (%)	34 (92)	21 (100)	0.180

*MAS and IAS continuous scores were recoded as compliant (all correct answers in the scale), and non-compliant (one or more mistakes).

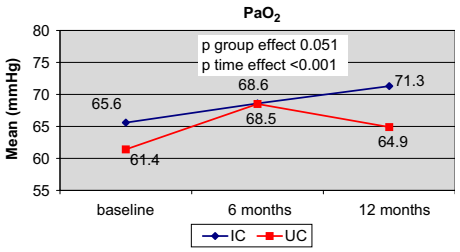

Figure 2 Changes in mean PaO_2 values (mmHg) along time, in UC ($n = 41$) and IC ($n = 21$) groups.

in the treated group.[23] The effects of poor adherence to treatment in COPD are not known, and it has been said that studies using adherence as an outcome should also measure clinical benefits.[24] Although we cannot attribute the reduction of the admissions risk[6] to any specific component or effect of the intervention, our data suggest that treatment adherence may have positive effects in COPD patients.

Nutritional status (as measured with body mass index) did not change in the UC group while it increased steadily in the IC group. We are not aware of any educational trial that measured nutritional status in COPD patients. Since there were no undernourished patients (only 1 patient had BMI $\leqslant$ 20), nutritional advice of our intervention was directed to avoid overweight. The difference at 12 months, although small in absolute numbers (1.34 kg/m^2), could be due to the higher rate of admissions during the follow-up period in the UC group, which would have had a negative effect on nutritional status. One limitation of the study was the lack of measurement of fat free mass index.

The lack of change in lung function after 1 year of intervention is consistent with previous findings of educational[7,8] or home based care[25–27] programmes, and plausible given the natural history of COPD.[28] However, we found that pulmonary gas exchange improved in both groups until 6 months, something probably due to recovery after the exacerbation, and, from 6 to 12 months, worsened in the UC group while it improved in the IC group. One likely explanation is that the intervention leads to a better control of hypoxemia. However, the lack of differences in oxygen prescription and oxygen compliance between groups of treatment may rule out this possibility. Another explanation could be that changes in the course of the disease during the 12 months of treatment (such as exacerbations and admissions) are responsible for final values of pulmonary gases exchange. Existing literature does not help in understanding these findings, since none of the previous studies measured arterial blood gases, and only one study involving supported discharge intervention[26] found that oxygen saturation improved at 8 weeks in the treated group without changes in the control group.

We did not find differences in general (Euroqol) or specific (SGRQ) health-related quality of life (HRQL) measures, although both improved in both groups as a result of recovery after the exacerbation.[29] A meta-analysis of educational programmes in COPD did not find effects in the general HRQL, and only small effects in the specific HRQL measures.[7] Most of the home care or supported discharge programmes assessed their effect in specific HRQL, and only one found improvements after a short period of time,[11] while the remainder did not find effects after short,[26] medium,[27] or long periods.[25] Since trials of respiratory rehabilitation, which share some of the components with educational or home care based interventions, found an effect in quality of life,[21] it could be hypothesized that this effect is not attributable to "education" but to other components, among which "exercise" would be a key candidate, given the strong association between quality of life and physical activity in COPD patients.[30] In fact, a study which included self-management and exercise training without supervision in COPD[8] found improvements in the impact subscale of the SGRQ at 4 months but not at 12 months, their difference between groups being lower than what we found in symptoms.

The lack of differences in pharmacological prescriptions between UC and IC groups suggests that adherence to international guidelines in severe COPD after a hospital admission, is acceptable in our area. In addition, treatment of co-morbidities at 12 months was scored as correct in 100% of patients both in the UC and IC group. We did not find changes in smoking or physical activity habits related to the intervention, probably because of a ceiling effect.

Main limitations of the present study are the small sample size and the high proportion of patients lost to follow-up. The study sample size was computed to answer the primary objective of reduction in admissions in all subjects included in the trial, but unfortunately only part of the patients (those from Barcelona) had information about changes in risk factors. Even then, sample size was very similar to previous educational or home care intervention studies. We tested the degree of selection bias by comparing characteristics of subjects lost to follow-up between the IC and UC groups. There was no relationship between variables that were different in these groups and outcome variables, reducing the possibility of selection bias as an explanation for the present results (data available from the authors). The extent to which our intervention can be exported to other subgroups of the COPD population or other health care systems is debatable and has been discussed elsewhere.[6] We conclude that, compared to UC, an IC programme including education, coordination among levels of care and increased accessibility, helped COPD patients to enhance knowledge and to influence health behaviour such as treatment adherence after 1 year of intervention. The interpretation of these findings together with the previously reported reduction in admission risk, suggest that these factors play an important role in the treatment of COPD exacerbations at an early stage, being able to reduce the need of hospital admission.

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RESUMEN DE LOS MANUSCRITOS

Home hospitalization of exacerbated chronic obstructive pulmonary disease patients

Los sistemas sanitarios pueden beneficiarse de nuevas formas de atención sanitaria más flexibles, que aumenten la eficacia del tratamiento de exacerbaciones graves de la EPOC, que requerirían ingreso hospitalario en un entorno asistencial convencional. En el estudio efectuado en 222 pacientes con exacerbación de la EPOC que acudieron a urgencias, se examinaron los resultados de un programa de hospitalización domiciliaria centrado en un modelo de atención integrada y basado en la atención de enfermería especializada y el soporte de TIC. Los pacientes que no presentaban criterios de hospitalización imperativa (definidos pre-hoc) fueron aleatorizados al grupo intervención (hospitalización domiciliaria) o a tratamiento convencional y reevaluados 8 semanas después.

Al final del período, los pacientes del grupo de hospitalización domiciliaria presentaron un menor número de visitas a urgencias, tuvieron una mejor calidad de vida, mejores índices de auto-control de la enfermedad y una mayor satisfacción de la atención comparada con el grupo de tratamiento convencional. Los costes directos globales fueron un tercio más bajos en el grupo de intervención, básicamente por una disminución significativa en el número de días de hospitalización.

Este es el primer estudio que demostró que la hospitalización domiciliaria fue coste-eficaz. Una intervención integrada de forma exitosa como ésta, cumplió además con dos de las premisas esperables: empoderó al paciente para el auto-control de su enfermedad y creó un apoyo compartido entre los distintos niveles asistenciales.

The impact of home hospitalization on healthcare costs of exacerbations in COPD patients

Las hospitalizaciones son responsables de aproximadamente el 70% de los costes atribuibles a la EPOC. Un programa de atención integrada domiciliaria en un grupo seleccionado de pacientes con exacerbación de EPOC demostró ser eficaz para disminuir la utilización de recursos asistenciales. El estudio utiliza la información de la primera publicación para

analizar el impacto de la hospitalización domiciliaria en los costes directos y evaluar el peso de los factores determinantes de los mismos. Un total de 180 pacientes del estudio anterior de los que se disponía de información completa en lo que respecta a utilización de recursos, fueron incluidos en el análisis de costes.

Los costes directos fueron significativamente menores en el grupo de hospitalización domiciliaria comparados con el grupo control, con una reducción del 35.8% equivalente a un ahorro promedio de 810€ por paciente durante los dos meses de seguimiento. A pesar de un aumento de los costes por medicamentos ambulatorios en el grupo intervención, los ahorros fueron obtenidos fundamentalmente a expensas de una disminución de los días de hospitalización. Las variables predictivas de un mayor coste fueron el deterioro de la calidad de vida, la alteración del FEV_1, el número de hospitalizaciones en el año anterior y pertenecer al grupo de tratamiento convencional. La magnitud del ahorro monetario atribuible a la hospitalización domiciliaria fue mayor en los pacientes más graves elegibles para este tipo de intervención.

A partir de la perspectiva del pagador, la sostenibilidad de este tipo de programas intensivos con objetivos muy específicos, estará determinada en gran parte por una contención de los costes semejante a la alcanzada. El modelo predictivo desarrollado, puede ser útil para estimar los costes y el retorno a la inversión de programas integrados de hospitalización domiciliaria.

Early Relapses After Severe Exacerbations in Patients with Chronic Obstructive Pulmonary Disease

Es bien conocido que un 25% de los pacientes hospitalizados por una exacerbación de la EPOC presentan recaídas que son motivo de reingreso en el período inmediatamente posterior al alta. Un programa de atención integrada domiciliaria en un grupo seleccionado de pacientes con exacerbación de EPOC demostró ser eficaz para disminuir la utilización de recursos asistenciales. Para el análisis, se definió recaída como la necesidad de hospitalización o la muerte. Para analizar los factores determinantes del riesgo de recaída, se estudiaron los mismos 222 pacientes del estudio de hospitalización domiciliaría descritos en el primer manuscrito. El análisis de regresión logística identificó que las variables que globalmente explican un deterioro de la calidad de vida (mal estado general, disnea severa, y un puntaje bajo en el dominio físico del SF-12), fueron las que se asociaron con una mayor riesgo de recaída. Un análisis secundario de los cambios observados durante las 8 semanas de seguimiento, mostró que un incremento en la actividad física y la mejoría de la oxigenación arterial se asociaron a un menor riesgo de recaída. Estos resultados permitirán identificar aquellos pacientes con alto riesgo de recaída y constituyen un apoyo para la toma de decisiones y la gestión de los programas de hospitalización domiciliaria. El papel modulador de la actividad física como protector del riesgo de recaída debe tenerse en cuenta como base de las intervenciones planteadas.

Integrated care prevents hospitalizations for exacerbations in COPD patients

La falta de datos sobre la eficacia de intervenciones encaminadas a prevenir hospitalizaciones por exacerbación de EPOC en pacientes clínicamente estables probablemente está condicionada por la heterogeneidad de los pacientes incluidos y la falta de estandarización de las intervenciones propuestas. Una atención integrada y de carácter distributivo entre los distintos niveles asistenciales y apoyados en TIC puede generar resultados positivos, en términos de reducción de la utilización de recursos asistenciales. Un total de 155 pacientes con una exacerbación de EPOC fueron reclutados al momento del alta hospitalaria, y posteriormente aleatorizados a atención integrada o a cuidado convencional. El estudio se efectuó en Barcelona y Leuven, con un seguimiento de 12 meses. La intervención al grupo de atención integrada consistió en caracterizar el paciente al momento del alta para diseñar un plan individualizado de seguimiento que sería compartido con el equipo de atención primaria, y ofrecerle accesibilidad a una enfermera especializada gestora de casos a través de un centro de llamadas articulado con una plataforma tecnológica basada en internet que facilitaba la interrelación entre niveles asistenciales.

Después de un año de seguimiento, los pacientes de atención integrada tuvieron una menor tasa de hospitalizaciones y un mayor porcentaje de días libres de hospitalización que el grupo control. La mortalidad y la utilización de otros recursos asistenciales: llamadas telefónicas y visitas al médico, fueron semejantes entre los dos grupos. Este es el primer estudio, que demuestra la eficacia de una intervención basada en la articulación de los recursos existentes entre la atención primaria y el hospital para prevenir hospitalizaciones no planeadas por episodios de exacerbación de la EPOC.

Effects of an integrated care intervention on risk factors of COPD readmission

La atención integrada de pacientes con EPOC descrita en el estudio anterior fue eficaz para disminuir el número de hospitalizaciones no planeadas durante 1 año de seguimiento. En el último manuscrito de la tesis, se evalúa la eficacia de dicha intervención para generar cambios en la calidad de vida, el estilo de vida y el auto-control de la enfermedad que podrían explicar la reducción en las hospitalizaciones descrita. Se analizaron un total de 113 pacientes del protocolo anterior correspondiente al sub-estudio de Barcelona, quienes tenían toda la información clínica necesaria para el análisis.

Después de un año de seguimiento, los pacientes del grupo de intervención mejoraron el índice de masa corporal y las variables educativas relacionadas con el auto-control de la enfermedad (conocimiento de la EPOC, identificación de los signos de alarma de exacerbación, inicio temprano del tratamiento de las exacerbaciones, adherencia en el uso de inhaladores y una técnica correcta en el uso de los mismos). La atención integrada mejoró el conocimiento de la enfermedad y la adherencia al tratamiento, lo que sugiere que empoderar al paciente en el autocontrol de la enfermedad genera cambios conductuales que podrían asociarse a un menor riesgo de hospitalizaciones por exacerbación de la EPOC.

DISCUSIÓN

La discusión de los resultados de esta tesis, se ha estructurado alrededor del análisis de las fortalezas y debilidades de los programas de atención integrada evaluados. Sin embargo, para el análisis de cada uno de los temas propuestos, la EPOC debería considerarse como un caso de uso útil para la validación de intervenciones semejantes en otras enfermedades crónicas que compartan cursos clínicos afines. La generalización de estos resultados, generará valor al modelo planteado y aportará herramientas de comparación para futuras intervenciones a gran escala.

La discusión se ha dividido en cuatro apartados:

1. Análisis crítico de los resultados obtenidos
2. Limitaciones asociadas a la evaluación de los costes
3. El papel facilitador de las TIC en la implementación del nuevo modelo
4. Los retos de la extensión del modelo en los sistemas sanitarios

Análisis crítico de los resultados obtenidos

La necesidad de replantear los sistemas de atención sanitaria para atender la carga que generan las enfermedades crónicas obliga a introducir cambios fundamentales en la estructura de los servicios asistenciales, siguiendo las orientaciones descritas en la introducción. Los programas de atención integrada evaluados en esta tesis doctoral se han diseñado como una respuesta a necesidades específicas. Creemos que los resultados pueden añadir valor a la construcción de esquemas novedosos de atención para los pacientes con EPOC y alto riesgo de hospitalización por episodios de exacerbación. Asimismo, consideremos que los nuevos esquemas tienen potencial para modular aquellos aspectos del pronóstico de la enfermedad relacionados con las exacerbaciones graves.

Estudio hospitalización domiciliaria

Eficacia

Sin demeritar el éxito de otros programas de hospitalización en el domicilio[90-92;128] y alta temprana[93] en términos de seguridad y reducción de costes durante las exacerbaciones

de la EPOC, nuestro estudio fue el primero en demostrar su eficacia para evitar nuevas visitas a urgencias, mejorar la calidad de vida y el auto control de la enfermedad y generar una contención de los costes.

Sin embargo, ninguno de estos estudios de intervención domiciliaria pudo evitar la elevada frecuencia de reingresos hospitalarios en los dos meses posteriores al alta, que fluctuó entre un 25% y 35% de los casos. Siendo estos porcentajes muy semejantes a los encontrados en la práctica clínica convencional[64;129;66], se puede asumir que el tipo de intervención domiciliaria prestada durante las intervenciones no afectó el riesgo posterior de reingreso. Por lo tanto, es posible que otros factores, no tenidos en cuenta durante los estudios, hubiesen modulado el riesgo de reingreso hospitalario, como: a) la gravedad global de la enfermedad de base; b) estrategias de tratamiento durante y después de la exacerbación; y, c) la fragmentación de la atención sanitaria.

a) Gravedad de la EPOC. La selección de candidatos constituye un aspecto fundamental que condiciona los resultados obtenidos. En nuestro estudio de hospitalización domiciliaria fueron excluidos los pacientes con necesidad imperativa de hospitalización (apoyados por los criterios recomendados por la British Thoracic Society[130]), aquellos que presentaban co-morbilidades activas severas o no controladas y aquellos sin soporte social. Los criterios de exclusión referidos generan sin duda un sesgo que debe tenerse presente en el momento de diseñar una generalización de este tipo de servicio. En los pacientes aleatorizados, las variables asociadas con un mayor riesgo de reingreso, como la frecuencia de hospitalizaciones durante el año anterior, los niveles de hipoxemia e hipercapnia y una mayor severidad de la obstrucción[131] fueron semejantes en los dos grupos. Ello refuerza la validez interna de los resultados. Es posible que una caracterización más completa y multidimensional de la gravedad de la EPOC hubiera permitido identificar otros factores relacionados con la gravedad que, en teoría, podrían haber influido en el desenlace alcanzado, como serían: la inactividad física[64;82;132;133] y los efectos sistémicos de la EPOC[134], ambos asociados a una mayor utilización de recursos sanitarios. Sin embargo, el diseño del estudio con aleatorización a ciegas da pocas oportunidades a un sesgo debido a dichos factores.

b) Estrategias de tratamiento. Los cambios inflamatorios en la vía aérea durante la exacerbación[135;136] han sido relacionados con una recuperación lenta y un mayor riesgo de recaída de la exacerbación. Dado que en el estudio se siguieron las recomendaciones internacionales para el tratamiento de exacerbaciones severas[137,138-140] cabe pensar que las posibilidades de optimización de este apartado son reducidas. Un aspecto limitante del estudio es que no disponemos de información sobre el momento en que fue iniciado el tratamiento antibiótico antes de la consulta al servicio de urgencias. Este aspecto puede ser de interés, teniendo en cuenta que el inicio temprano de la terapia con antibióticos, cuando está indicada, se asocia con una resolución más rápida de la exacerbación[74]. Como hemos comentado anteriormente, la reducción de la tasa de re-hospitalización en la EPOC (y otras enfermedades crónicas) es una asignatura pendiente. La mejora de los cuidados

transicionales post-alta constituye una futura área de trabajo abierto a la evaluación de nuevas intervenciones que permitan reducir los reingresos. Entre ellas, la necesidad de iniciar los programas de rehabilitación pulmonar inmediatamente después de los episodios de exacerbación[141]. También el tratamiento de niveles elevados de dióxido de carbono ($PaCO_2$) han sido asociados con un mayor riesgo de mortalidad[66] y de reingreso hospitalario[142;143], tanto en exacerbaciones tratadas médicamente ó a las asociadas con el uso de ventilación mecánica no invasiva en la fase aguda[144]. Los datos de nuestro tercer manuscrito refuerzan la importancia de la actividad física precoz y del tratamiento de la hipoxemia después del alta hospitalaria.

c) Fragmentación de la atención. Es razonable pensar que la fragmentación entre niveles asistenciales puede ser una causa de la elevada tasa de reingresos descrita en la literatura. Incluso en nuestro estudio, el nivel de integración entre el equipo de hospitalización domiciliaria y el de atención primaria fue mejorable. La intervención fue liderada por el equipo del hospital de tercer nivel, enviando información regular al nivel primario, pero sin establecer una real interacción entre los distintos niveles asistenciales. Tal como propone el MCC, los dispositivos de atención deben ser liderados por profesionales de atención primaria que pertenecen a las Redes Regionales de Cuidado Integral, quienes deben ser las encargadas de coordinar la estrategias de colaboración estrecha entre los niveles asistenciales, definiendo entonces el concepto de modelo distributivo de atención sanitaria[14;103].

En este escenario planteado, las nuevas propuestas para la atención de pacientes con EPOC en programas de hospitalización domiciliaria o alta temprana, requiere un mayor conocimiento de los factores clínicos (caracterización de la EPOC y de las exacerbaciones) y sociales que puedan predecir una mayor probabilidad de éxito para este tipo de intervención. Su conocimiento, enmarcado en una estrategia de atención integrada de carácter distributivo con roles muy bien definidos de los profesionales y sus responsabilidades, debe augurar desenlaces exitosos no solo a nivel del dispositivo de hospitalización domiciliaria sino también en la reducción de la tasa de re-hospitalizaciones. En realidad, los resultados del estudio de prevención de hospitalizaciones (manuscritos 4 y 5) refuerzan este planteamiento.

Validez

Como se describió en el manuscrito 1, el método de asignación de los sujetos en el grupo intervención o control se efectuó mediante un proceso de aleatorización ciega. El inicio del estudio con una relación de aleatorización de 2:1 favor del grupo intervención debe considerarse como una medida conservadora para alcanzar un mayor volumen de pacientes en dicho grupo. El posterior cambio a una relación 1:1 no compromete en absoluto la capacidad de comparar ambos grupos.

Entre los factores que generan un elevado nivel de validez interna de los resultados cabe señalar el pequeño porcentaje de pérdidas de información durante el período de segui-

miento (< al 2%) y la estandarización de la intervención realizada durante su estancia en el hospital y en el domicilio del paciente.

Por la naturaleza misma de su diseño como experimento clínico, la generalización de los resultados debe ser analizada con cautela, en la medida en que sólo se le impone validez externa a los resultados, si ellos pueden reproducirse en otras latitudes bajo condiciones semejantes. Debemos reconocer que existen al menos dos factores: el elevado porcentaje de exclusiones y la alta movilidad de los pacientes dentro de nuestro sistema sanitario, que pueden limitar la validez externa de los resultados. Ambos aspectos se discuten con detalle en el manuscrito. Un elemento en sentido contrario son los buenos resultados de la utilización de este modelo de hospitalización domiciliaria como práctica asistencial convencional del Hospital Clínic a partir de finales del 2006.

Al tratarse de un estudio orientado al tratamiento de una enfermedad específica (EPOC), se excluyó un alto porcentaje de pacientes que fueron considerados como frágiles, sea por la presencia de co-morbilidades graves o bien por insuficiente soporte social o logístico en el domicilio del paciente, que impedían la implementación de la intervención.

La presencia de co-morbilidades aumenta el riesgo de muerte en los pacientes con EPOC[27;145-147], comparado con el que le impone la misma exacerbación per se[68]. El elevado impacto de las co-morbilidades en la cronicidad y las características de las asociaciones más frecuentes en la EPOC (cardiopatía crónica, diabetes tipo 2 y cáncer)[48] plantean la evidente necesidad de construir guías de atención por agrupaciones de enfermedades frecuentes (guías orientadas al paciente)[46] que sustituyan a las guías clínicas convencionales orientadas a una única enfermedad.

Se ha comentado que otro de los factores importantes de exclusión se refiere a aquellos pacientes con insuficiente soporte social o logístico debido a falta de apoyo de la red familiar o social cercana al domicilio. También se refiere a aquellos pacientes que teniendo cuidador no disponían de las condiciones mínimas necesarias para realizar este tipo de servicios en el domicilio, como por ejemplo no tener teléfono en el hogar o ser analfabetos. En el estudio de hospitalización domiciliaria no se contemplaba un apoyo social y comunitario en el domicilio. Cabe señalar que entre las directrices del MCC se incluye una integración del sistema sanitario con la red social comunitaria como respuesta a este tipo de desventajas observadas en determinados grupos poblacionales. Este aspecto deberá ser contemplado cuando se plantee la extensión y sostenibilidad de este tipo de servicios sanitarios.

La heterogeneidad de los pacientes crónicos, según gravedad de la enfermedad dominante, impacto de las co-morbilidades y necesidades de soporte social, exige la necesidad de estratificación de acuerdo con estos factores determinantes del perfil de riesgo de los pacientes. Dado este primer paso, el siguiente debe centrarse en rediseñar los procesos de atención integrada alrededor de ellos mismos y no sobre patologías específicas. Los

nuevos programas de atención integrada orientados a pacientes crónicos dibujarán un sistema sanitario con más énfasis en la prevención, más inclusivo y ante todo con una respuesta más integral a las necesidades actuales de la sociedad.

La elevada movilidad de los pacientes dentro del sistema sanitario constituye un factor que, en teoría, podría tener un impacto sobre la validez externa de los resultados obtenidos en el programa a hospitalización domiciliaria. En muchos países europeos, existe una sobresaturación de los servicios de urgencias de los grandes hospitales, principalmente durante los períodos invernales. Ello sucede a pesar de los esfuerzos organizativos de las autoridades sanitarias para que la consulta inicial se efectúe al médico de atención primaria y se limite la derivación o el acceso espontáneo a los servicios de urgencia de los hospitales.

En España, en el marco de un análisis transversal efectuado durante el Estudio de los Factores de Riesgo de Agudización de la EPOC (EFRAM) se objetivó que más de dos tercios de los pacientes admitidos por una exacerbación en un hospital de nivel terciario (~70%) se habían auto-referido desde el domicilio hacia los servicios de urgencias de los hospitales, sin pasar por el filtro del nivel primario de atención[148]. Ello contrasta con la realidad observada en otros países como el Reino Unido en que esta proporción es mucho más baja y puede variar entre el 1 y el 30% de los pacientes[90]. La facilidad para el acceso directo de los pacientes a los servicios de urgencias puede estimular la utilización de esta sin necesidad objetiva de una atención especializada. No sería aventurado especular que una atención inicial ambulatoria por el médico de primaria pudo haber evitado una hospitalización innecesaria. Cabe señalar que esta posibilidad no excluye, a nuestro entender, los beneficios potenciales adicionales de un programa de hospitalización domiciliaria liderado por el hospital con un enfoque integrado que, además, tenga una buena interacción con la atención primaria.

Estudio prevención de hospitalizaciones

Eficacia

Los episodios de exacerbación de la EPOC continúan siendo una de las mayores causas de hospitalizaciones no planeadas, principalmente en pacientes frágiles con co-morbilidades e insuficiente soporte social. La eficacia para prevenir hospitalizaciones por exacerbación grave de la EPOC ha sido muy controvertida. Mientras algunos estudios mostraron resultados negativos[149;150], otras intervenciones aisladas enfocadas en el auto-control de la enfermedad, han demostrado prevenir hospitalizaciones y mejorar la calidad de vida[95;151;152]. Estos resultados, sugirieron que la variabilidad en la eficacia preventiva, estaba condicionada por la heterogeneidad de los pacientes involucrados, por la insuficiente estandarización de las intervenciones propuestas y por la utilización aislada y fraccionada de alguno de los elementos del MCC, sin aprovechar las bondades de todo el modelo integral[119].

En nuestro estudio, la intervención consistió en diseñar y compartir un plan individualizado de seguimiento con el equipo de atención primaria y la enfermera del hospital a través de una plataforma tecnológica que apoyaría la interrelación entre todos los niveles asistenciales. Después de un año de seguimiento, los pacientes aleatorizados al grupo de atención integrada tuvieron una menor tasa de hospitalizaciones y el porcentaje de pacientes vivos que no habían reingresado fue mayor, que el grupo de cuidado convencional. La eficacia comprobada para prevenir hospitalizaciones puede evaluarse de varias formas:

a. La tasa global de reingresos durante el seguimiento, fue menor en el grupo de intervención. Además, se observaron los mismos resultados cuando el análisis se hizo por separado para Barcelona y Leuven. Ello permite especular que dadas las diferencias entre los dos sistemas sanitarios (ver más adelante), los cambios observados en el estudio se deben a la intervención y están poco condicionados por las especificidades de cada sistema sanitario.

b. La comparación realizada entre la frecuencia de hospitalizaciones durante el año de seguimiento y el año anterior a la intervención en el mismo sujeto, fue una medida adicional de la eficacia de la intervención. Siendo el paciente su propio control, el valor que tiene la intervención para demostrar sus beneficios es mucho más valiosa, por la connotación de individualización de los procesos asociados para alcanzar los desenlaces esperados.

No obstante, siendo las estrategias de los modelos de atención integrada multifactoriales (educativas, coordinación entre los distintos niveles asistenciales, accesibilidad fácil, etc.), es difícil cuantificar la asociación entre los desenlaces alcanzados y el efecto modulador de cada uno de los factores involucrados en la estrategia de atención integrada. Consideramos que este aspecto es poco importante dada la relativa simplicidad de la intervención efectuada. En este estudio, los pacientes del grupo intervención alcanzaron un mejor auto-control de la enfermedad posterior a la intervención: mayor conocimiento de su patología y los signos de alarma y una mayor adherencia al tratamiento. Estos datos sugieren que estos cambios conductuales jugaron un papel relevante en la prevención de las exacerbaciones de EPOC. Con toda probabilidad, los pacientes del grupo intervención fueron capaces de detectar de forma precoz las exacerbaciones y desencadenar medidas de auto-control efectivas o bien buscar ayuda por medio de los canales de accesibilidad articulados, en especial el centro de llamadas.

Validez

De acuerdo con lo descrito en forma detallada en el manuscrito, el proceso de asignación de los sujetos a los grupos de estudio no fue el mismo en los dos centros (Leuven y Barcelona) por una transitoria aleatorización de pacientes con una relación 1:2 (control e intervención, respectivamente) en Barcelona debido a necesidades de la logística del

estudio. Ello provocó un desequilibrio en el número final de sujetos en cada grupo (n=65 para el grupo de intervención y n=90 para el grupo control), sin efecto alguno sobre la validez interna y externa de los resultados.

Debido a las diferencias encontradas en los grupos en el momento de entrada en el estudio (el número de hospitalizaciones el año anterior fue mayor y la frecuencia de sujetos vacunados contra virus de influenza fue menor en el grupo control) fue necesario hacer un ajuste en el análisis estadístico. La consistencia de los datos fue garantizada con un análisis de las hospitalizaciones durante los dos años anteriores al estudio en los pacientes del grupo de Barcelona. No hubo pérdidas de pacientes durante el seguimiento, a excepción de los fallecidos o aquellos que alcanzaron algún criterio de exclusión. Todas estas razones nos permiten considerar una elevada validez interna de los resultados alcanzados.

De acuerdo con el diseño del estudio, la intervención propuesta tuvo que ser adaptada a las especificidades de los sistemas sanitarios catalán y belga, respectivamente. Estas diferencias y la adaptación de la intervención a las dos realidades se analizan a continuación:

a. El estudio fue realizado en Barcelona y Leuven, dos ciudades europeas con sistemas sanitarios muy distintos para el modelo de atención integrada propuesto. Barcelona es una ciudad grande y muy poblada que vive al ritmo de metrópoli. El hospital de referencia en el estudio está ubicado en un sector urbano que cubre un área de referencia relativamente pequeña, de fácil acceso, pero muy poblado (unos 540.000 habitantes). Por el contrario, Leuven, es una ciudad pequeña más tranquila y cercana a Bruselas, con un hospital ubicado en un sector urbano mucho menos denso, que cubre un área de referencia rural muy grande y de acceso difícil por las distancias. Como ya se comentó, mientras en Barcelona, el 70% de los pacientes que acuden al servicio de urgencias son auto referidos desde el domicilio, en Bélgica, condicionados por las grandes distancias ya descritas, los médicos de atención primaria deben prestar una atención domiciliaria intensa y lejos de los grandes hospitales, filtrando la posibilidad de que los pacientes se auto-refirieran al hospital. En Bélgica, los médicos de atención primaria actúan como “guardianes de puertas” o “gate keepers” del sistema de salud.

b. Las características diferenciales de los dos escenarios (Leuven y Barcelona) obligaron a adaptar las intervenciones. Por un lado, mientras la intervención inicial en Barcelona, entre la enfermera especialista del hospital y el equipo de atención de la primaria fue realizada en el domicilio del paciente, con un talante más “personalizado”, en Leuven esta visita no fue realizada por las distancias. En la ciudad belga, la intervención domiciliaria no fue efectuada de forma sistemática y el estudió consistió en una formación y soporte remoto del médico de atención primaria por parte de enfermería especializada del centro hospitalario de referencia. De acuerdo con la organización del sistema sanitario belga, las visitas domiciliarias durante el año de seguimiento por parte de los médicos de atención primaria fueron relativamente frecuentes, a diferencia de Barcelona en que las visitas no planeadas al domicilio o en el hospital día fueron mínimas.

La intervención inicial en el hospital (en el momento del alta), fue semejante en las dos ciudades. Además podemos aceptar que se consiguió una estandarización de la intervención durante el seguimiento a pesar de las adaptaciones que tuvieron que ser realizadas debido a las diferencias sanitarias y geográficas descritas. Las modificaciones de la estructura de la intervención no distorsionaron su esencia, ni la de sus componentes, sino que por el contrario, creemos que enriquecieron el estudio. Obligó a los miembros del equipo, a adaptarla a las necesidades del sistema y del paciente, convirtiendo una aparente debilidad en fortaleza para las especificaciones del MCC.

En Leuven, donde por naturaleza los médicos de la primaria visitan regularmente el domicilio del paciente, el número de visitas fue muy semejante en los dos grupos. Se puede asumir, por tanto, que el valor añadido se debe a la implementación de la intervención por parte de los médicos. En Barcelona por el contrario, probablemente el peso de la visita domiciliaria, la accesibilidad al centro de llamadas y las muy ocasionales visitas en el domicilio por parte de la enfermera, fueron los responsables del éxito.

A nuestro entender, la eficacia de los resultados obtenidos en este estudio tienen un valor muy importante para el diseño de nuevas intervenciones que permitan modificar el curso clínico de las exacerbaciones de EPOC. Fueron pilares básicos del éxito de la intervención, la articulación de los recursos existentes entre la atención primaria y el hospital. En definitiva, el estudio constituye una muestra de que el modelo distributivo de atención alcanzó los objetivos esperados y evitó duplicidades. En Leuven, el médico de primaria lideró la integración entre los niveles, mientras en Barcelona lo logró la enfermera. Con los resultados alcanzados, puede asumirse que independientemente del profesional que asuma el liderazgo a nivel de la primaria, mientras los roles y las competencias necesarias sean adquiridas y asumidas, los desenlaces finales serán alcanzados. En todos los casos, debe existir una buena articulación de los recursos existentes (modelo distributivo).

Finalmente, el soporte de las TIC fue esencial para aumentar la accesibilidad y evitar la fragmentación de la atención, compartir información entre los niveles y acceder a herramientas educativas basadas en evidencia para los profesionales, pacientes y la comunidad. Cabe señalar que el aumento de accesibilidad no implicó ningún abuso en la utilización de recursos disponibles. En este sentido, creemos que existen dos explicaciones: el destinar este tipo de intervenciones a grupos diana con criterios de inclusión/exclusión bien delimitados y estandarizar adecuadamente las intervenciones en lo que respecta a flujos de trabajo entre los actores (pacientes vs profesionales y profesionales vs profesionales).

Limitaciones asociadas a la evaluación de los costes del modelo

La ausencia de parámetros que definan una estructura de negocio para la sostenibilidad de este tipo de intervenciones de atención integrada, se constituye en uno de los principales factores limitantes para una implementación a gran escala. El impacto económico

de este tipo de intervenciones en el cuidado de los pacientes pueden valorarse desde la perspectiva de coste-eficacia, explorando si el coste económico de la inversión es sostenible para la sociedad, y desde la perspectiva del beneficio, explorando el retorno de la inversión en el tiempo, evaluado como ahorro del sistema a largo plazo y como eficacia de los desenlaces clínicos alcanzados. El coste desde un punto de vista social se refiere al valor de los recursos empleados, que no necesariamente son monetarios, en la prestación de un servicio o en la ejecución de un proceso[153].

Los estudios de evaluación de costes deben incluir en todos los casos, bajo qué perspectiva se implementó su diseño, el tipo de costes que analizó y el tipo de análisis de costes que utilizó. Como la elección de la perspectiva determina el rango de costes que deberán ser incluidos en el análisis, es indispensable conocer si se hizo desde la perspectiva de la sociedad, del proveedor individual o grupo de proveedores no públicos, del sistema sanitario como asegurador o tercer pagador o si por el contrario fue desde la perspectiva del paciente, donde los costes relevantes deben ser aquellos que le afectan directamente su bolsillo y las pérdidas de productividad que repercuta en una disminución salarial[154].

En nuestro estudio (manuscrito 2), los costes fueron calculados desde la perspectiva del pagador, en este caso la seguridad social pública de la ciudad de Barcelona (Consorcio Sanitario de Barcelona-Hospital Clínic), y por esta misma razón sólo se incluyeron los costes directos tangibles, los fijos que no se modifican a pesar del tipo de intervención y los variables que cambiaron de acuerdo con los suministros. Se escogió hacer un análisis de minimización de costes teniendo en cuenta que los datos provenían de un estudio controlado de eficacia de una intervención. En este tipo de análisis se comparan los costes de dos o más alternativas terapéuticas cuyos desenlaces clínicos sean iguales o sin diferencias estadísticamente significativas para grupos de pacientes en condiciones similares[155]. Así mismo, su hipótesis se catalogó como de dominancia débil, es decir aquella que asume que la diferencia de desenlaces es nula, pero la de costes es positiva a favor de la intervención que se plantea[156]. Sin querer alejarnos de los beneficios demostrados, pero buscando las limitaciones que pueda tener este análisis en el futuro, es evidente que si individualizamos el impacto económico generado para cada uno de los proveedores implicados en nuestro modelo de atención, la inequidad podría hacerse muy evidente. Por ejemplo, siendo los costes de los medicamentos en el grupo intervención más elevados que en el grupo control, pero menores que los costes de hospitalización, el proveedor llamado hospital ahorró (en términos de necesidades de estructura) al disminuir la estancia hospitalaria, mientras el proveedor llamado farmacia domiciliaria gastó más recursos en medicamentos. En nuestro estudio, el pagador fue el mismo, pero puede no ser semejante en otras latitudes.

Se identificaron 3 variables predictoras de un coste (ahorro) más elevado que, a su vez contribuyen a definir la gravedad de la EPOC[27]: a) una mayor obstrucción al flujo de aire espirado (menor FEV_1); b) un elevado número de hospitalizaciones por exacerbación en el año anterior; y, c) una peor calidad de vida. Esta asociación directa entre la gravedad de

la EPOC y los costes, permitió generar un modelo predictivo del coste en función de ellas y el grupo de atención al que pertenecieron. Este tipo de diseños, permitirá presupuestar los costes de la inversión realizada, al involucrar cohortes de pacientes con gravedad conocida en programas de atención integrada, y asegurar así la sostenibilidad financiera del sistema.

El cálculo de los costes indirectos siempre será más complejo; sin embargo, para las nuevas modalidades asistenciales en donde se busca una mayor flexibilidad de los mismos, es obvio pensar en los gastos que generarán el desplazamientos de los servicios al domicilio del paciente de personal y tecnología, así como la movilización de cuidadores hacia y desde el domicilio del paciente cuando se evitan hospitalizaciones innecesarias, en donde el peso de los gastos versus el de los ahorros deben ser tenidos en cuenta. Así mismo, los costes por ausentismo laboral y falta de productividad del paciente y/o del cuidador tampoco deben ser olvidados[154].

El papel facilitador de las TIC en la implementación del nuevo modelo de atención sanitaria

Es innegable que uno de los pilares fundamentales para facilitar los cambios que se avecinan con el desarrollo y la implementación de los nuevos modelos emergentes de atención sanitaria, son las TIC[124;157]. La evidencia sugiere que mejoran la calidad de los procesos de atención y disminuyen el uso inadecuado y redundante de los recursos asistenciales, al mejorar la transferencia de información alrededor de las guías de cuidado de los pacientes. Ello permite optimizar la supervisión y monitorización de actividades y señales biológicas y disminuye el riesgo potencial de errores[158].

Globalmente la salud electrónica conocida como e-salud (e-Health), se refiere al uso combinado de tecnología informática y comunicación electrónica de información digital sanitaria para propósitos clínicos, educativos o administrativos sanitarios, sean locales o a distancia[159;160]. En el marco de la implementación de un modelo de atención sanitario para el cuidado de los pacientes crónicos como el MCC, este tipo de herramientas pueden dar respuesta a las necesidades administrativas y financieras de los sistemas y pueden ayudar a estructurar la gestión de los procesos clínicos de atención[99].

Bajo esta perspectiva, en los dos estudios de esta tesis se utilizaron las TIC dentro del proyecto CHRONIC[127]. Esta plataforma se diseñó para facilitar la gestión de los pacientes y aportar herramientas de trabajo colaborativo entre los profesionales de los niveles asistenciales. Actividades estandarizadas que formaron parte del modelo de atención, no pudieron haber sido operativas en ausencia de una plataforma como lo fue CHRONIC. De la misma forma, si esas actividades generaron cambios conductuales a través de los procesos de autocontrol adquiridos por el paciente, podemos especular que la plataforma fue el instrumento de apoyo de los resultados clínicos obtenidos.

Sin embargo, la falta de interoperabilidad de los diferentes componentes del sistema para poder trabajar conjuntamente, ha sido una de los limitantes identificados para una futura utilización extensa de los nuevos modelos de atención sanitaria para paciente crónicos. En este contexto, el desarrollo de plataformas tecnológicas intermedias, con software abierto y diseño modular, que permitan esa interoperabilidad con los sistemas de información de diferentes proveedores puede que ofrezca soluciones para evitar la fragmentación del cuidado de los pacientes si se adoptan los cambios organizativos necesarios. En el futuro, este tipo de plataformas además de ser elementos de soporte para gestionar servicios innovadores de atención integrada, ofrecerán valor añadido como herramientas de generación de conocimiento y apoyo específico en la toma de decisiones de los profesionales y de los pacientes[161].

Los retos de la extensión del modelo en los sistemas sanitarios

La estratificación de los sujetos o pacientes en función del riesgo, la gravedad de la enfermedad, la fragilidad y el pronóstico, debe ser una de las funcionalidades planteadas para la extensión del modelo. Asimismo, el aumento progresivo en la carga que generan las enfermedades crónicas, ubica dos escenarios adicionales no enfocados estrictamente en pacientes con enfermedades crónicas avanzadas y alto riesgo de recaídas, como los analizados en nuestros estudios:

a. Los pacientes con enfermedad leve y la población general a riesgo de padecerlas. Siendo los sistemas sanitarios los responsables sociales de la salud de las personas, un enfoque más centrado en la prevención primaria y ante todo más incluyente con programas y estrategias más proactivas son necesarias. Este escenario, tiene una mayor trascendencia, al saber que más del 50% de las enfermedades podrían haber sido evitadas con cambios en estilo de vida. Los perfiles de disminución de prevalencia de algunas de estas enfermedades crónicas (i.e cardiovasculares) en los países desarrollados son indicativos del potencial existente para conseguir una prevención efectiva. Si bien las enfermedades cardiovasculares representaron aproximadamente el 20% del total de las AVISAs, es conocido que al menos dos terceras parte de ellas pudieron haber sido evitadas con estrategias encaminadas a buscar estilos de vida más saludables (actividad física regular, dieta adecuada y evitar la exposición al tabaco), que ayuden a modular la historia natural de este tipo de patologías. Para ellos se adoptará un patrón asistencial muy centrado en la capacidad de auto-gestión y el empoderamiento de la enfermedad con un bajo impacto sobre el sistema sanitario. Los programas de rehabilitación pulmonar, vistos como intervenciones centradas en el paciente, con intervención física, psicológica y educativa que genera cambios del comportamiento, pueden ser un excelente ejemplo para este tipo de escenarios, cumpliendo además con todos los preceptos que el MCC propone[162;163].

b. La evolución de pacientes con enfermedades crónicas estables pero complejas, que ameritan necesidades muy diversas, más relacionadas con prevención terciaria en el

domicilio. Tal es el caso de pacientes con SIDA, hoy considerada una enfermedad crónica y de los pacientes con trasplante de órganos. Este escenario plantea la necesidad de desarrollar programas de tercer nivel asistencial en el marco de la atención primaria localizados en el domicilio, pero con un sólido soporte del especialista[14].

En este tipo de escenarios personalizados, el futuro nos deparará grandes avances en la mayoría de las enfermedades crónicas, en lo que se relaciona con manifestaciones clínicas, control de recaídas y exacerbaciones, atenuación del impacto y mejora en el pronóstico; por ejemplo en la EPOC, la gestión de las exacerbaciones graves dejaría de ser el elemento central de la enfermedad, y las hospitalizaciones por su causa serían la excepción, sobretodo en pacientes frágiles y con reingresos muy frecuentes; las intervenciones tempranas diseñadas en base a un mayor conocimiento de los mecanismos íntimas de las enfermedades crónicas permitirían modular el curso de las mismas y mejorar el pronóstico de forma substancial.

Bajo todas estas perspectivas, es posible visionar que los factores limitantes para la extensión e implementación de este tipo de modelos pueden ser:

a. El cambio organizativo dentro de los sistemas sanitarios: acostumbrados a un *vis a tergo* entre las fuerzas renovadoras con visión de cambio y las tradicionales aferradas al modelo clásico y centralizado de atención sanitaria, los sistemas tendrán que buscar estrategias novedosas para generar estos cambios. Los estrategas líderes de las instituciones deben ser capaces de reconocer la naturaleza de los mismos, y explotar en su personal las oportunidades que este nuevo paradigma de atención les impone. Estas oportunidades podrán alcanzarse en sistemas sanitarios más transversales y menos jerárquicos en donde el hospital y la primaria jueguen roles y funciones complementarias y no excluyentes alrededor del cuidado del paciente. Esta integración entre los niveles asistenciales, debe apoyarse en elementos como la cultura de la organización, la visión y la misión del modelo de atención propuesta y la estrategia sanitaria planteada. También debe apoyarse en los sistemas de información como elemento coordinador de apoyo a los procesos, transmisor de las guías de atención y de material educativo para pacientes y para los profesionales, que les permita apoyar la autonomía en la toma de decisiones de cada día[14].

b. Los nuevos roles y la preparación de los profesionales: un cambio estructural sin modificar los roles y la preparación de los profesionales tiende al fracaso. La identificación de las nuevas competencias de los profesionales para acoplarse al sistema, y ejercer sus funciones con calidad y seguridad debe ser los objetivos prioritarios para la implementación[164]. Las competencias que deben adquirir deben centrarse en aprender cómo pasar de un cuidado reactivo a uno proactivo, aprender a negociar con el paciente planes individualizados de cuidado que tengan en cuenta sus necesidades, aprender a soportar los esfuerzos continuados para mantener el auto-control de los pacientes, aprender a coordinar los grupos de trabajo multidisciplinarios, y trabajar

como miembro de un equipo de atención y como líder en la comunidad[165].

c. El modelo de negocio: El modelo de atención integrada necesita de la interacción de diversos tipos de proveedores públicos o privados no institucionales en un sistema de competitividad cooperativa perfectamente factible en un marco de cobertura sanitaria pública con una cartera de servicios bien definida. La multiplicidad de interacciones entre actores frecuentemente agrupados en diferentes sistemas de provisión de servicios debe ser posible con un retorno razonable de la inversión realizada[109], sin generar fragmentación del sistema de salud. En estos momentos, los modelos de negocio que faciliten la sostenibilidad y la extensión a gran escala de nuevos servicios de atención integrada están aún poco desarrollados[166].

Las estrategias de desplegamiento de este tipo de modelos dependerán también de la confluencia de experiencias acumuladas en los estudios clínicos considerados inicialmente como pilotos. La relativa inmadurez de los programas de atención integrada para pacientes crónicos, no ha permitido la generación de estudios sólidos de evaluación económica. A pesar de que la evidencia es cada vez más clara alrededor de las bondades de este tipo de intervenciones, muchos de los programas tienen una vida corta, porque nacieron de proyectos subsidiados o de protocolos clínicos de investigación sin una concepción de financiación a largo plazo, presupuesto y análisis de impacto de la inversión, que no permitirían implementarlos a gran escala. Estas propuestas finales no pretenden volver a refundar los sistemas sanitarios, imponiendo modelos de atención teóricos. Por el contrario, se trata de generalizar servicios de atención bien validados y estructurados que conlleven un cambio en la práctica clínica asistencial y en las interacciones entre la clínica, la investigación y la innovación tecnológica.

Con un enfoque holístico de la salud que incorpore los conceptos de atención integrada, se puede mejorar la funcionalidad de los sistemas y efectuar contención de costes. Este escenario, es probablemente el único adecuado para asegurar la viabilidad de unos sistemas de salud que sean sostenibles, contemplen un alto grado de accesibilidad y permitan incorporar los nuevos conocimientos generados en el ámbito de las ciencias de la vida[167].

RESUMEN

Las exacerbaciones graves de la EPOC son causa frecuente de hospitalizaciones no planeadas en pacientes con enfermedad avanzada. Este fenómeno se amplifica por factores como la existencia de co-morbilidades y el insuficiente soporte social que frecuentemente presentan estos pacientes. Los reingresos repetidos por exacerbaciones de la EPOC tienen efectos deletéreos sobre la calidad de vida de los pacientes, el progreso de la enfermedad y la mortalidad. Además, las hospitalizaciones tienen un peso importante sobre los costes totales de la EPOC y un impacto notable en el sistema sanitario.

El elevado grado de fragmentación de los sistemas sanitarios dificulta el desarrollo de políticas de prevención de eventos agudos adecuadas para los pacientes con enfermedades crónicas. Esta realidad plantea la necesidad de desarrollar un nuevo paradigma de la atención sanitaria basado en el desarrollo de servicios innovadores de atención integrada destinados a pacientes crónicos.

En la presente tesis doctoral propusimos dos nuevos servicios de atención sanitaria, destinados a la optimización de la atención de los pacientes con EPOC. El primer estudio analizó la eficacia de la hospitalización domiciliaria y alta precoz en pacientes que, en un modelo de atención convencional, habrían sido ingresados en el hospital. El segundo estudio evaluó el papel de una estrategia de atención integrada entre niveles asistenciales para la prevención de hospitalizaciones no planeadas en pacientes estables que presentan historia previa de ingresos hospitalarios repetidos por episodios de exacerbación de la EPOC.

La hipótesis central, común en ambos estudios, es que un modelo de atención integrada de carácter distributivo, centrado en el paciente, puede generar mejores resultados clínicos que la atención convencional, contribuir a la mejora del estilo de vida, adherencia al tratamiento de los pacientes y contribuir a la contención de costes. Un objetivo secundario ha sido el análisis del papel de la plataforma TIC desarrollado en el marco del proyecto CHRONIC como elemento de soporte de los servicios mencionados. Nuestra hipótesis de trabajo ha sido que las TIC son esenciales para facilitar la accesibilidad a pacientes y profesionales y constituyen un elemento básico para compartir la información en un modelo sanitario de carácter distributivo.

Bajo esta perspectiva, se diseñaron los dos estudios clínicos aleatorizados y controlados basados en intervenciones estandarizadas en los que se compararon los efectos de la

atención integrada en relación al tratamiento de carácter convencional tanto para la hospitalización domiciliaria (manuscritos 1-3), como para la prevención de hospitalizaciones no planeadas en pacientes clínicamente estables de alto riesgo (manuscritos 4 y 5). Los desenlaces fueron analizados en dos escenarios distintos. En la hospitalización domiciliaria, el estudio se efectuó en dos hospitales del área de Barcelona y tanto los pacientes como los controles fueron evaluados al ingreso y al cabo de 2 meses del alta. Las variables diana fueron: los días de ingreso en el hospital, el número de consultas al servicio de urgencias, los re-ingresos durante el período de seguimiento y la mortalidad. Fueron variables secundarias: la compresión y adherencia al tratamiento por parte del paciente y la utilización de recursos sanitarios. En el segundo estudio (prevención de hospitalizaciones), los pacientes fueron evaluados al inicio del estudio y a los 12 meses de seguimiento. Las variables diana en este caso fuero el número de ingresos hospitalarios y consultas al servicio de urgencias durante el año posterior a la inclusión en el estudio. Asimismo, se evaluaron los avances en el nivel de autogestión de la enfermedad y la contención de costes generada por el nuevo servicio. Dicho estudio se efectuó en Barcelona y en Leuven (Bélgica).

El estudio de hospitalización domiciliaria fue el primero en demostrar que la atención integrada fue coste-eficaz al alcanzar los objetivos esperados: a) un menor número de visitas a urgencias, b) mejor calidad de vida; c) cambios en el estilo de vida y mejor gestión de la enfermedad; y d) reducción de costes directos fundamentalmente relacionados con una disminución de los días de hospitalización, con un ahorro creciente para aquellos pacientes con enfermedad más grave elegibles para este tipo de intervención. El aumento de la actividad física durante el seguimiento, se asoció con un bajo riesgo de reingreso, lo que le sugiere su efecto modulador sobre un mejor desenlace clínico.

El estudio de prevención de hospitalizaciones demostró que la atención integrada alcanzó los objetivos esperados: a) una menor tasa de hospitalizaciones durante el período de seguimiento, comparado con el cuidado convencional, y b) un mejor conocimiento de la enfermedad y adherencia al tratamiento. Fue el primer estudio, que demostró en pacientes con EPOC, la eficacia de una intervención basada en la articulación de los recursos existentes entre la atención primaria y el hospital a través de una plataforma TIC. Asimismo, los resultados sugieren que empoderar al paciente en el autocontrol de la enfermedad puede generar cambios conductuales que disminuyan el riesgo de hospitalización por exacerbación.

Los resultados obtenidos son muy prometedores respecto a la eficacia del modelo asistencial. El potencial de desplegamiento a grupos seleccionados de pacientes crónicos es inmenso y muy halagador. Sin embargo, la limitada validez externa de los resultados obtenidos, condicionada por un elevado número de exclusiones de pacientes frágiles, postula la necesidad de involucrar programas transversales de atención, centrados en pacientes y no en patologías específicas, y el desarrollo de guías de atención que tengan en cuenta

las co-morbilidades más comunes. El fortalecimiento de los puentes de unión entre los pacientes, los profesionales y los servicios comunitarios de soporte social a través de las TIC facilitará la superación de la fragmentación de la atención sanitaria actual.

Los desarrollos futuros exigirán una adecuada estandarización de las intervenciones y la evaluación continuada de los resultados en un proceso de retro-alimentación. También se objetiva la necesidad de una adecuada estratificación de los grupos de pacientes diana de acuerdo a la gravedad y a otros factores que influyan en el pronóstico del paciente, como podrían ser las co-morbilidades. En definitiva, las propuestas de futuro deben incorporar una visión holística de la atención integrada, que incluya estrategias de atención a pacientes en fases iníciales de las enfermedades crónicas con el objetivo de modular el curso de las mismas y atenuar su impacto sobre el sistema sanitario.

CONCLUSIONES

De acuerdo con la hipótesis y objetivos planteados en esta tesis doctoral, los resultados obtenidos con los trabajos presentados, nos permiten concluir lo siguiente:

1. El programa de hospitalización domiciliaria basado en un modelo de atención integrada demostró eficacia clínica e impacto positivo sobre el estilo de vida y la autogestión de la enfermedad por parte de los pacientes. Asimismo, generó satisfacción en pacientes y profesionales. El análisis económico basado en el estudio de costes directos indicó un elevado potencial de ahorro en relación al tratamiento convencional.

2. Un modelo de atención integrada preventiva, que se basó en la articulación de los recursos existentes entre la atención primaria y el hospital, a través de una plataforma tecnológica basada en internet para prevenir hospitalizaciones no planeadas por episodios de exacerbación de la EPOC, demostró su eficacia al disminuir la utilización de recursos asistenciales.

3. Una intervención estructurada, estandarizada, centrada en el paciente y compartida por todos los actores de modelo para grupos seleccionados de pacientes, parece ser la clave del éxito de este tipo de modelos integrados. El apoyo de las TIC debe valorarse como una herramienta indispensable para su implementación.

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ANEXO 1
EDITORIAL
Integrated care: a new model for COPD management?
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EDITORIAL

Integrated care: a new model for COPD management?

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Total healthcare expenditure in countries of the Organisation for Economic Co-operation and Development has risen from an average of 5% of gross domestic product in 1970 to ~10% in 2002 [1]. In 2002, pharmaceutical expenditure ranged from 10% of the total healthcare expenditure in Sweden to 21% in France [1], and a major portion of this expenditure arose through hospital care. Chronic obstructive pulmonary disease (COPD) is one of the most common chronic diseases worldwide [2] and a common cause of hospitalisation. An analysis of the economic cost of COPD in the UK shows that 54% accrues from hospitalisation; a further 32% is equally divided between scheduled care and drug treatment [3]. The Study of Risk Factors of COPD Exacerbation (EFRAM Study) showed that among a wide range of potential risk factors, only previous admissions, lower forced expiratory volume in one second, and the under-prescription of oxygen are independently associated with a higher risk of admission for a COPD exacerbation [4]. Under-prescription of home oxygen is easily modifiable once hypoxia has been diagnosed, but hospital admission rates for COPD remain a challenge for pulmonologists and chest therapists alike. In the current issue of the *European Respiratory Journal*, there is a new and interesting attempt at management of the severe COPD patient. CASAS *et al.* [5] advance a model that may have great potential for the cross-cultural modification of hospitalisation rates for COPD. Previous studies have shown that self-management of COPD within the community can reduce hospitalisation [6] and exacerbation severity [6, 7]. The economic efficacy of these models is unknown, but since hospitalisation contributes the greatest proportion of costs for COPD, models targeting patients at risk for hospitalisation may be expected to have the widest appeal to chest physicians and healthcare providers alike.

Several attempts have been made at establishing interventions for patients with chronic illnesses, almost all of which include prevention of hospitalisation as an outcome measure and almost always within one cultural environment. A meta-analysis of 102 such studies has shown that commonly used interventions have included patient education, healthcare provider education, and provider feedback. All such studies were associated with improvements in disease control and adherence to practice guidelines, but because of the diversity of outcome measures and structure, little else could be concluded [8]. In COPD, such studies have recruited patients from the community or hospital. The East London COPD study, a long-term cohort study of moderate-to-severe COPD patients in the community, showed that over a period of 6 yrs hospitalisation rates were higher amongst those COPD patients who tended not to seek treatment for an exacerbation compared with those who sought early treatment from family physicians or the study clinicians [7]. BOURBEAU *et al.* [9] studied 191 COPD patients of similar severity recruited from the outpatient clinics of seven Canadian hospitals, randomised to a self-management plan or usual care (UC), and showed that self-managed subjects were less likely to be hospitalised during the first and also the second year, when there was less contact with the study team [6]. While the East London study looked at unselected patients in the community, the study by BOURBEAU *et al.* [9] required prior hospitalisation in the previous year as a prerequisite [7, 9]. However, a randomised study of self-management *versus* UC involving 248 COPD community-based patients from the Netherlands showed no measurable beneficial effects of self-management on quality-adjusted life years, or health-related quality of life, but this study did not require prior hospitalisation as a prerequisite and the patients were of milder severity than in either of the previous two studies [10]. This suggests that perhaps self-management programmes should focus on the more severe patients who tend to use most resources.

In order to decrease the cost of hospitalised patients, supported discharge or hospitals at home schemes have been advocated. Where generic management home-based schemes have been used for chronic disease patients, no benefit has been found for COPD [11–14]. A Scottish observational study of 962 patients with COPD also found benefit for hospital-led home-based care [15], but a recent Australian randomised controlled study found no benefit [16]. However, the number of randomised controlled trials using this approach has been relatively small. In a systematic review, RAM *et al.* [17] found seven such trials involving a total of only 754 patients, but were able to conclude that home-based schemes are associated with cost savings as well as decreased hospitalisation. All of these studies have used differing models, but commonly involve a respiratory therapist or senior nurse case manager. Furthermore, in a systematic review of nine randomised controlled trials of inpatient, outpatient and community-based interventions (excluding hospital at home and early discharge schemes), TAYLOR *et al.* [18] have cautioned that even though the data are sparse, there is currently little evidence to support purely nurse-led management interventions for COPD.

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CASAS *et al*. [5] utilised an innovative approach for this problem, and several features of this study are of interest. First, the authors studied hospitalised COPD patients in two different cultural environments, Belgium and Spain. Secondly, apart from including a specialised nurse case manager, they incorporated a chronic platform, which was a web-based application that facilitated phone calls to the case manager, as well as record keeping *via* phone calls, home visits or home video conferencing. In a study of 217 adults with type-2 diabetes, GLASGOW *et al*. [19] concluded that physicians and patients were willing to participate in computer-assisted diabetes self-management and that results appeared robust over various patient and delivery characteristics. A small study from Athens (Greece) has also suggested that telemedicine home support of severe COPD patients may decrease hospitalisations [20]. The use of computer-assisted care for chronic diseases has been slow in coming, but will receive greater attention during this decade and the authors should be commended for having the foresight to use this increasingly available resource in their methodology.

Unlike hospital-led home-based studies, the hospital stay of patients in the study by CASAS *et al*. [5] was not truncated by access to the study as patients were recruited at discharge determined by local protocols. However, at discharge, there was careful evaluation for access into the study as well as a 2-h educational session. The case management was customised to location. Thus, in Belgium, general practitioners (GPs) were included *via* regional education sessions and were specifically contacted by one of the researchers; however, in Spain, there was one joint visit involving the case manager and the primary care team within 72 h of discharge. Phone calls were made weekly for 1 month, then at 3 and 9 months. The study showed that this integrated care (IC) model is effective in preventing hospital admissions with specifics adapted to differing local health environments. The study did not include evaluation of GP training in Belgium where there was a greater emphasis on GP involvement. However, the frequency of GP visits did not differ between the UC or IC arms, and, since the IC arm was associated with better outcomes, this may be taken as indirect positive evaluation of GP training in the Belgium arm of the study.

Some limitations, as well as implications, of the study should be mentioned. Deaths in both the UC and IC arms were similar, with the majority being from end-stage pulmonary disease. However, there was no evidence of differences in death rates from exacerbations of COPD in either arm, although this was not an outcome measure of this study and should be a matter for careful evaluation in further studies. CASAS *et al*. [5] have explained in some detail why the randomisation process was altered in one of the centres, but this does not appear to have biased the results. With the fall off in frequency of programmed phone calls with time, the intensity of case manager involvement would be expected to decline. The effect of this aspect of the study design on hospitalisation rates was not assessed during the study, but it should be noted that hospitalisation rates in the second year when contact times had fallen were unaffected in the Canadian study alluded to earlier [6]. Interestingly there were no home visits of the case manager in Belgium due to the geographical dispersion of the patients, but home visits were part of the protocol in Spain, yet the hazard ratio for hospitalisation at Belgium was 0.35, compared with that of 0.52 in Spain. Thus, one of the inferences from this study is that where there is good communication with primary care, there may be no need for home visits from secondary or tertiary care facilities.

One further important question that all healthcare providers will want to ask is which patients should be enrolled into these programmes? The major problem with community-recruited self-management models is that they have a recruitment rate of only 50% [6, 9], whereas supported discharge and IC models originating within hospitals have a much higher recruitment rate: CASAS *et al*. [5] had a refusal of only 3%. One apparently disappointing feature of the study is that only 19% of admitted patients met the stringent inclusion criteria. The study required home visits and thus the 39% of patients not in the catchment area had to be excluded and, quite reasonably, a further 10% who were illiterate could not be included, as they had to be able to make use of the chronic platform. A further 32% with severe comorbidity who probably required a separate IC pathway were also excluded. Obviously, the exclusion of 39% of patients because of the catchment area can represent a potential source of bias, but we may be reassured that these patients differed in being only slightly more likely to be females and less likely to be smokers than those included; importantly, they did not differ in severity as measured by the need for intensive care. Thus, the integrated pathway of care is available for all COPD patients, without significant comorbidity, provided they are literate.

The main message of the study is that an integrated care pathway with flexible shared-care arrangements between primary care and hospital, facilitated by information technologies, has an enormous potential to decrease hospital admissions in chronic obstructive pulmonary disease patients. In the integrated care approach, several models are available and we now require comparative studies. However, we must also be aware that from a healthcare provider perspective, further studies of this model must include cost-effectiveness as well as effectiveness in older disabled patients with chronic obstructive pulmonary disease.

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