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Tesis Doctoral

OPTIMIZACIÓN DE LA GESTIÓN DEL STOCK EN FARMACIA HOSPITALARIA

STOCK MANAGEMENT OPTIMIZATION IN HOSPITAL PHARMACY

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INTRODUCCIÓN

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1.1. Gestión de Inventarios en Farmacia Hospitalaria

La Farmacia Hospitalaria se encarga de la adquisición, control, selección, preparación, dispensación e información de medicamentos y productos sanitarios, entre otras actividades orientadas al uso seguro y efectivo de los mismos, en los pacientes atendidos en el centro y en su ámbito de influencia. El carácter urgente de muchos medicamentos y el hecho de facilitar el acto único en las dispensaciones a pacientes externos que acuden a consulta hacen imprescindible la disponibilidad de medicamentos en cantidad suficiente para atender la demanda. De hecho, la no disponibilidad de medicamentos en cantidad adecuada podría tener consecuencias fatales, pudiendo conducir incluso a la pérdida de vidas humanas.

1.1.1. Retos de la gestión de inventarios

Un Servicio de Farmacia de hospital lleva a cabo una importante labor de gestión de stocks con el fin de satisfacer las necesidades clínicas del hospital, lo que requiere, por un lado, abastecer a todas las unidades asistenciales como plantas de hospitalización, quirófanos, consultas, urgencias, hospital de día, etc. y, por otro, cubrir la dispensación a pacientes externos que retiran medicación de uso hospitalario y de diagnóstico hospitalario sin cupón precinto, todo ello manteniendo los medicamentos en condiciones adecuadas de conservación y caducidad. Además, existen diversos condicionantes que dificultan esta tarea:

- **Impredecibilidad de la demanda.** Sólo la actividad programada y la estacionalidad en el consumo de algunos medicamentos permiten predecir parcialmente la actividad esperada. La programación de intervenciones, de ingresos para administración de medicación en régimen ambulatorio y de las dispensaciones de pacientes externos estables, sin cambios y sin revisión próxima, permiten anticiparse a las necesidades futuras para aprovisionar medicamentos. De la misma manera existen determinados medicamentos cuyo comportamiento estacional puede ser aprovechado para mejorar la estimación de su demanda. Sin embargo, esta información no es suficiente para planificar de forma general la adquisición de medicamentos debido a que la actividad clínica de un centro hospitalario es dinámica y no puede programarse nunca por completo a causa de las urgencias hospitalarias, los ingresos no programados y los cambios de tratamiento tanto de pacientes ingresados como externos que acuden a revisión.

- **Dependencia de los proveedores.** El mantenimiento del stock depende siempre del abastecimiento y adecuado servicio de múltiples proveedores. Ningún centro está exento en cualquier momento de un retraso en la entrega o de una rotura de stock de un determinado medicamento. De hecho, cada vez son más los desabastecimientos temporales producidos por la industria farmacéutica a los que los Servicios de Farmacia deben hacer frente en el día a día buscando alternativas, ya sea otro proveedor, otra presentación de mayor o menor dosis o bien otro medicamento similar del mismo grupo terapéutico siempre que no existan contraindicaciones. Como última opción en estos casos se contempla también la petición de préstamo a otro hospital que disponga del medicamento en cuestión. Esta práctica puede ser útil entre hospitales cercanos y en días laborables siempre que se pueda utilizar algún transporte propio del centro, pero puede tener un elevado coste cuando se realiza entre hospitales alejados o de distintas ciudades incluso o en días festivos. Además, no sólo hay que contabilizar el coste de la recogida del centro que lo cede, sino la devolución posterior al restablecimiento del suministro.

- **Aversión a las roturas de stock.** Por todos los motivos anteriormente expuestos se establece un *stock de seguridad*, que nos permite hacer frente a la incertidumbre introducida por estos factores y cubrir la demanda del centro a pesar de las posibles discontinuaciones de suministro, demoras en las entregas o fluctuaciones de la demanda. Es decir, estas variabilidades se tratan de compensar de alguna manera con un aumento de stock medio, y por tanto de los costes. En este punto cabe destacar que el stock de seguridad no garantiza completamente el abastecimiento, aunque sí minimiza sustancialmente el número de eventos de rotura de stock que pueden surgir ante posibles imprevistos.

- **Costes.** En todos los centros, y sobre todo en las circunstancias actuales, existen restricciones económicas y presupuestarias que obligan a priorizar y optimizar los recursos disponibles. Es muy importante procurar una adecuada rotación de stocks que reduzca en lo posible la inmovilización de medicamentos y su consiguiente caducidad. Es importante resaltar que el coste económico de algunos de los medicamentos de los que dispone un Servicio de Farmacia de Hospital llega a los varios miles de euros por unidad. De hecho, el valor inmovilizado en medicamentos puede suponer un tercio del presupuesto de un centro hospitalario [42] y hasta un 35 % de las compras en bienes y servicios en un hospital provienen del Servicio de Farmacia [3].

- **Caducidades.** Los medicamentos caducados suponen una pérdida económica en sí mismos por la necesidad de una nueva compra para su sustitución. No obstante, la gestión de estos caducados también consume tiempo del personal. Esta tarea consiste en revisar el stock, retirar todo aquello caducado o próximo a caducar y proceder a su destrucción por las vías adecuadas o a su devolución al laboratorio con el consiguiente acondicionamiento del paquete, además de dar salida informática de esas unidades. Se trata de una actividad necesaria e imprescindible de realizar en todos los centros y que se traduce en tiempo del personal, además del coste de envío de medicamentos a los proveedores en su caso. Este tiempo y coste se incrementan cuando se trata de estupefacientes, medicamentos que requieren un especial control en su adquisición, dispensación y devolución, siendo necesario un vale oficial para efectuar estos movimientos. Es por ello que una gestión que reduzca las caducidades de los productos resulta más productiva y ventajosa para el aprovechamiento de los recursos.

- **Restricciones de almacenamiento.** Hay que tener en cuenta que el espacio disponible para el almacenamiento restringe el número máximo de unidades que pueden ser almacenadas. Aunque cada vez está más extendido el uso de robots y sistemas automatizados de medicamentos con un aprovechamiento máximo del espacio, no deja de ser una limitación y es preciso adaptar el stock al espacio disponible. Además, estos sistemas de almacenamiento automatizados requieren una gran inversión y no todos los centros disponen de ellos, sobre todo los centros pequeños. Por otra parte, esta necesidad de espacio es especialmente significativa en el caso de medicamentos que requieren refrigeración. Además de los medicamentos termolábiles clásicos como las insulinas, los bloqueantes neuromusculares, las vacunas, ciertos citostáticos, etc. hay que añadir los nuevos anticuerpos monoclonales de uso en diversas enfermedades autoinmunes, que cada día son más frecuentes y numerosos. Los frigoríficos o cámaras frigoríficas tienen una capacidad de almacenamiento limitada, lo que supone una restricción considerable, además del coste de adquisición y mantenimiento de los mismos.

- **Recursos humanos disponibles.** Por último, los recursos humanos en un Servicio de Farmacia también son limitados. El hecho de formalizar pedidos requiere tiempo para mecanizarlos y para recepcionarlos informáticamente una vez servidos:

    - *Pedidos.* Las existencias y la actividad hospitaria determinan qué medicamentos hay que pedir. Para ello hay que introducir los códigos en el sistema informático, determinar las unidades a solicitar, comprobar el proveedor y si exige importe mínimo de pedido y formalizarlo. En caso de que requiera un importe mínimo hay que completar el pedido con otros artículos del mismo proveedor, aumentando así el tiempo dedicado por cada línea introducida. En este caso, además, puede producirse un almacenamiento excesivo de determinados medicamentos que ayudan a llegar a ese mínimo imprescindible, pero que realmente no hay necesidad de pedir. De ahí la importancia de planificar muy bien qué se pide y cuánto en cada momento. Existen, además, casos particulares que aumentan de forma significativa la carga de trabajo del personal en este sentido, a saber:

        - Especialidades extranjeras. Cada vez con más frecuencia se producen desabastecimientos de la industria farmacéutica que se prologan en el tiempo. Los Servicios de Farmacia los resuelven solicitando especialidades extranjeras importadas cuya adquisición es aprobada por parte del Ministerio de Sanidad y Consumo. Estas solicitudes requieren unos trámites especiales que constan de una solicitud formal a través de una aplicación específica que justifique mediante un informe la necesidad del medicamento en cuestión. Es la Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) la que autoriza y da conformidad al suministro.

  - Distribuciones controladas. En muchas ocasiones la baja disponibilidad de determinados medicamentos por parte del proveedor obligan a una distribución controlada del mismo, y en estos casos su gestión pasa a realizarse también a través de esta aplicación comentada. Para su solicitud es necesario aportar un informe médico que justifique la necesidad del tratamiento y que el paciente cumple los criterios establecidos por la AEMPS para acceder al mismo. Es competencia de la AEMPS autorizar finalmente o no el suministro.
  - Estupefacientes. Lo mismo ocurre con los estupefacientes cuya compra requiere además del envío de un vale oficial sin cuya recepción no se entrega el pedido.

  En estos casos la gestión de solicitudes y pedidos de medicamentos conlleva por parte del farmacéutico más tiempo aún y más trámites de lo habitual. De ahí la importancia de una buena política de gestión que tenga un aprovechamiento máximo de recursos.

- *Recepciones.* Al margen de la ejecución del pedido, la recepción informática también consume tiempo del personal al comprobarse la coherencia del pedido recibido con lo solicitado, la coincidencia del precio en aquellos albaranes valorados y la mecanización del lote y caducidad en el sistema. Tampoco puede obviarse el tiempo que implica la recepción y el correcto almacenamiento teniendo en cuenta fechas de caducidad, por ejemplo, o adecuando el almacén para mercancía de gran volumen como los sueros.
- *Indicencias.* Inevitablemente, derivadas de los pedidos y sus recepciones se producen incidencias como pueden ser la solicitud de un código nacional dado de baja o sustituido por otro, la solicitud de medicamentos con problemas de suministro o incluso la no recepción del pedido en el proveedor, además de discordancias de precios, de unidades recibidas

o de medicamentos enviados. Estas incidencias deben ser resueltas de inmediato, sobre todo aquellas que afectan al producto recién solicitado. La no resolución puede implicar que el medicamento no se sirva o que se produzca una demora en su entrega.

Resumiendo, una buena política de stocks debe basarse en estrategias de compra que, por un lado, satisfagan las necesidades clínicas y aseguren la cobertura de la demanda con cierto grado de certeza en un determinado periodo de tiempo, minimizando la cantidad de producto almacenado y respetando así las restricciones impuestas tanto por el espacio de almacenamiento y el stock máximo almacenable, como por los recursos económicos y humanos [41, 30].

1.1.2. Técnicas de gestión de inventarios

Como puede verse, la gestión de stocks es un problema complejo que requiere establecer un equilibrio entre objetivos diferentes y contrapuestos como son la necesidad de garantizar el abastecimiento y la minimización de la utilización de los recursos económicos y humanos del hospital. Por ejemplo, si se aumenta la frecuencia de pedidos para satisfacer la demanda y se reduce al mismo tiempo la cantidad solicitada para no excederse en el presupuesto, se multiplica la carga de trabajo del personal, lo que acaba siendo contraproducente. La complejidad de este problema se ve incrementada por factores externos como retrasos en las entregas o la variabilidad de la demanda que obligan a establecer un stock de seguridad.

En este contexto es, por tanto, importante establecer además de una política de stocks eficiente en la utilización de recursos en términos humanos y económicos, que determine qué pedir, cuánto y con qué frecuencia, que tenga en cuenta todas estas limitaciones con las que desarrollan su labor los Servicios de Farmacia de hospital. Con ese objetivo, históricamente, los Servicios de Farmacia han utilizado diversas técnicas y además se han propuesto en la literatura diferentes métodos de gestión que persiguen la minimización de los costes de almacenamiento mientras la demanda se satisface sin retrasos [23, 16, 15, 27]. Algunas de las más destacadas se citan a continuación:

- **Análisis ABC**. Consiste en clasificar los artículos inmovilizados según su valor económico siguiendo la distribución de Pareto: en el grupo A se incluyen aquellos artículos que representan en torno a un 15 % del total en cuanto a unidades pero un alto porcentaje (alrededor del 75 %) del capital del stock total, en el grupo B se incluyen aquellos que suponen en torno a un 20 % en unidades y alrededor de un 20 % del capital, y en el grupo C aquellos que representan la mayor parte del stock en unidades (alrededor del 65 %) y solamente un pequeño porcentaje del capital (un 5 % aproximadamente). Según esta clasificación la mayor parte del valor económico del stock inmovilizado se encuentra en un pequeño porcentaje del stock total. Es por ello que puede ajustarse la frecuencia de los pedidos en función de la importancia económica de cada grupo. En concreto, a mayor peso económico se asigna mayor frecuencia, lo que permite reducir tanto la cantidad pedida como el nivel medio de inventario de estos medicamentos.

- **Técnica del punto de pedido**. Consiste en ejecutar un nuevo pedido cuando el stock baje de un determinado valor x y se hará de la cantidad restante hasta un stock máximo prefijado X. Este método hace diferentes asunciones, como por ejemplo plazos de entrega fijos y una distribución de la demanda tipo Gaussiana [35, 6].

- **Lote económico de compras. [39, 1]** Consiste en repetir pedido de una determinada cantidad siempre que el stock llegue al mínimo establecido. Se asume en este caso que la demanda y los plazos de entrega son variables estocásticas.

- Otras políticas relacionadas que tratan de resolver estas cuestiones se encuentran en obras como [5].

No obstante, la mayoría de estas estrategias de gestión tratan de simplificar ignorando las cuestiones abordadas anteriormente y que suponen importantes limitaciones en el día a día de un Servicio de Farmacia. Se han desarrollado algunas alternativas por ejemplo en [10, 12, 7, 29]. Sin embargo, en general, estos métodos asumen una demanda constante, sin roturas de stocks ni retrasos en el reparto, y no tienen en cuenta todos los factores que rodean a la problemática de la gestión de stocks. Por ello, estas simplificaciones se han mitigado a costa de aumentar los niveles de stock con un stock de seguridad o bien se han implementado soluciones sobre el comportamiento de la demanda. No obstante, las decisiones tomadas, dado que se desconoce el riesgo asumido realmente, pueden conducir a considerar valores de stock de seguridad subestimados que no cubran del todo la demanda o bien a puntos de pedido ineficientes.

1.2. Hipótesis y Objetivos

Dadas la problemática existente y la dificultad de disponer de una buena política de gestión de stocks por las diversas limitaciones que hemos comentado, y teniendo en cuenta que la implementación de estrategias eficientes de gestión puede conllevar importantes ahorros económicos [11, 14], el objetivo final de la presente tesis doctoral es la optimización y la implantación de nuevos sistemas que mejoren la eficiencia de la gestión en Farmacia Hospitalaria.

Hoy en día, el uso de las nuevas tecnologías y la creciente información disponible facilitan el uso de técnicas más sofisticadas para abordar estas cuestiones que limitan la gestión de stocks [19, 4, 22, 2, 21, 36, 40, 17, 9]. Concretamente, este proyecto propone el desarrollo y aplicación de técnicas avanzadas de predicción y control orientadas a la problemática que rodea a la gestión de stocks en un Servicio de Farmacia.

Partiendo de la hipótesis de que los históricos de datos almacenados contienen información relevante para caracterizar la demanda de cada uno de los medicamentos y la política de pedidos, los objetivos de este trabajo son los siguientes:

1. Obtener métodos fiable de previsión de la demanda de medicamentos que facilite la planificación y la gestión de stocks.

2. Automatizar en la medida de lo posible la realización de los pedidos mediante la creación de un sistema de soporte al farmacéutico que aprenda de los datos históricos y de los nuevos datos generados de la actividad diaria.

3. Validar las políticas propuestas tanto en simulación como en el propio hospital.

1.3. Métodos

Los métodos empleados en esta tesis doctoral pueden diferenciarse también en función de los objetivos anteriormente indicados.

1.3.1. Métodos para la previsión de la demanda

La demanda juega un papel esencial y es desconocida a priori por el Servicio de Farmacia. En esta tesis doctoral se estudian nuevos sistemas de estimación de la demanda de manera que se pueda disminuir su incertidumbre. Partiendo de la información de históricos reales de un hospital (datos de consumos, roturas de stock, dispensaciones, pedidos, stocks…), se establecen las correlaciones correspondientes con el consumo esperado de medicamentos. Más aún, algunos de los métodos de gestión empleados se alimentan directamente de estos datos históricos y los utilizan como escenarios para la toma de decisiones. Una correcta estimación de la demanda reduce la incertidumbre en las necesidades de salidas de almacén que se van a producir en un periodo de tiempo, con lo que permite anticipar el consumo futuro, pudiendo disminuir el stock de seguridad con la consiguiente reducción de stock medio, redundando en un menor stock inmovilizado, una menor necesidad de almacenamiento y, en definitiva, en un ahorro económico.

1.3.2. Métodos para la gestión de inventarios

La mejora en la estimación de la demanda se utilizará para hacer previsiones y se aplicará al estudio de nuevas políticas de gestión en Farmacia Hospitalaria y su validación real en un hospital. Se pretende diseñar un sistema de optimización de la gestión mediante la evolución de los niveles de stock basada en los históricos comentados y así implementar un sistema de soporte a la decisión para la gestión. En este sentido y, a diferencia de los métodos clásicos de gestión, el sistema desarrollado no realizará ningún tipo de hipótesis simplificadora sobre la distribución de la demanda sino que lleva a cabo los cálculos directamente con datos. Concretamente se llevarán a cabo simulaciones para evaluar diferentes métodos de Control Predictivo Basado en Modelo[1] aplicados al control de los niveles de

[1] Es habitual referirse a esta metodología como *MPC*, como acrónimo del inglés *Model Predictive Control*.

stock de un Servicio de Farmacia Hospitalaria real. El MPC es una estrategia de alto rendimiento, muy popular para el diseño de controladores basados en modelos debido a su capacidad de manejar interacciones entre distintas variables, restricciones en las variables controladas y requerimientos de optimización de un modo sistemático. Se trata de un método de control muy versátil con múltiples aplicaciones en la industria y en diversos campos, que utiliza un modelo matemático del sistema para predecir su evolución como una función de la secuencia de acciones implementadas en un determinado horizonte de tiempo [8].

Las relaciones causa/efecto que se producen en los sistemas pueden ser caracterizadas mediante modelos matemáticos. El conocimiento del modelo que caracteriza el sistema permite calcular acciones de control sobre el sistema para que éste se comporte como deseamos. El MPC emplea el modelo del sistema para calcular las acciones óptimas de control desde el punto de vista de una cierta función definida a lo largo de un horizonte temporal de N pasos hacia el futuro. En cada instante de tiempo discreto se calcula la actuación óptima para los próximos N pasos para que el sistema siga a la referencia de acuerdo con la función y se desecha el resto. Es decir, que el MPC realiza un recálculo constante de las acciones de control en cada instante de tiempo de acuerdo a la información más reciente disponible, optimizando la secuencia de acciones o estados futuros de un sistema a lo largo de un horizonte dado.

Las dificultades que presenta la gestión de stocks son fácilmente modelables en el marco de las técnicas de MPC. De hecho, ha sido considerado en múltiples ocasiones como una estrategia adecuada para este tipo de problemática y se ha empleado con éxito tanto en la industria como en cuestiones similares [37, 38, 33, 25, 13, 20, 28, 24, 32, 31, 34].

Estas técnicas explotan directamente datos para optimizar las acciones futuras, los niveles de stock en este caso, a lo largo de un horizonte de tiempo dado, considerando restricciones en las variables del sistema y la incertidumbre de la demanda. Por ello, junto a los datos históricos de consumos, a partir de las estimaciones disponibles acerca del comportamiento esperado de la demanda e introduciendo una serie de restricciones en un modelo matemático, como embalaje, tiempo de entrega, pedido mínimo, stock máximo almacenable, stock mínimo necesario, precio de compra, etc., el sistema podrá predecir la evolución del stock. Adicionalmente, se probará también a predecir la probabilidad de rotura de stock con un nivel de riesgo controlado.

1.4. Publicaciones relacionadas con la tesis doctoral

A continuación, se comentan de forma cronológica las diferentes publicaciones obtenidas a lo largo de esto años y que de alguna manera han conducido a la elaboración de la presente tesis doctoral. Cabe destacar que la doctoranda es coautora de todos los trabajos que se enumeran y que su rol dentro de los mismos ha ido ganando protagonismo con los años. En este sentido, las primeras publicaciones se corresponden con colaboraciones académicas entre la Universidad de Sevilla y el hospital Reina Sofía, donde ocupaba una plaza en formación de Especialista de Farmacia Hospitalaria. Es a partir de la participación junto con la Escuela Técnica Superior de Ingenieros de la Universidad de Sevilla en el proyecto *Pharmacontrol*, financiado por la Junta de Andalucía y en el que la doctoranda participa como responsable del Servicio de Farmacia del Hospital San Juan de Dios de Córdoba, cuando se entiende que la aplicación de métodos avanzados de gestión de inventarios y previsión de la demanda supone una oportunidad de gran interés científico e industrial, motivo por el cual se inscribe en el Programa de Doctorado de Farmacia de la Universidad de Sevilla con el objetivo de realizar una tesis doctoral en esta temática. Por tanto, el peso específico de la doctoranda y su contribución son mayores en los artículos obtenidos en esta última etapa. Por todo ello, es posible clasificar las publicaciones en dos grandes grupos, a saber, aquellas que preceden a esta tesis doctoral y aquellas contribuciones que conforman la contribución científica propiamente dicha de la tesis.

1.4.1. Publicaciones anteriores a la tesis doctoral

Sin más preámbulos se procede a la enumeración de publicaciones de la doctoranda que preceden a la tesis doctoral:

1. El primer trabajo en el que se aplicaron técnicas de MPC a la gestión de stock en Farmacia Hospitalaria fue desarrollado en una comunicación oral

para el congreso de la Sociedad Andaluza de Farmacia Hospitalaria 2010, titulada "*Impacto económico de la aplicación de técnicas de control predictivo basado en modelo a la gestión de un Servicio de Farmacia*". Se aplicó una metodología en simulación muy básica a dos medicamentos en cuestión partiendo del histórico de datos reales de un hospital de entradas y salidas de los mismos en el periodo de estudio. Este trabajo podría ser catalogado como una prueba de concepto que sirvió para ilustrar las posibilidades de la aplicación del control predictivo en este contexto. Asimismo, cabe destacar que fue una de las 3 comunicaciones escogidas para su presentación oral en el congreso.

2. Dados los prometedores resultados obtenidos en la comunicación anteriormente comentada, se continuó ampliando la investigación. En primer lugar, se estudian nuevas técnicas de estimación de la demanda sin realizar ningún tipo de hipótesis simplificadoras sobre su distribución, sino directamente en base a datos históricos. En "*Análisis y minimización del riesgo de rotura de stock aplicado a la gestión en farmacia hospitalaria*" (Farmacia Hospitalaria 2011) se determina el valor que debería tomarse como stock de seguridad en un medicamento concreto estudiado y seleccionado por su alto coste y por la inmediatez de su necesidad en la actividad diaria de un hospital real. Este stock de seguridad se establece en función del nivel de riesgo y del número de días que se desee resistir sin rotura de stock. Adicionalmente se calcula también el valor que debería tomar dicho stock conforme a diferentes reglas utilizadas por los Servicios de Farmacia y se comparan con el método propuesto.

3. Se estudia también la minimización del riesgo de rotura de stock mediante diferentes métodos en "*Control predictivo aplicado a la gestión de stocks en farmacia hospitalaria: un enfoque orientado a la minimización del riesgo*" (Revista Iberoamericana de Automática e Informática industrial 2013). En particular, se aplica el MPC en simulación con datos reales de un hospital desde una perspectiva de minimización del riesgo. Se añaden acciones de mitigación con el objetivo de reducir el impacto de los posibles riesgos que pueden ocurrir. Por lo tanto, se añaden al problema inicial nuevas variables

de decisión.

4. En el artículo para el congreso Emerging Technology and Factory Automation 2014, titulado "*Optimizacion of the demand estimation in hospital pharmacy*" se analizan y comparan diferentes métodos de estimación de la demanda, incluyendo el método habitual usado en los hospitales.

5. Esta mejora en la estimación de la demanda permite a continuación estudiar nuevas técnicas de optimización de stock. Específicamente se evalúan y comparan 3 técnicas de gestión diferentes basadas en MPC en un trabajo presentado en el congreso Emerging Technology and Factory Automation 2014, titulado "*Application of robust model predictive control to inventory management in hospitalary pharmacy*".

6. En la comunicación para el congreso Conference on Decision and Control 2014, titulada "An application of chance-constrained model predictive control to inventory management in hospitalary pharmacy" se aplican restricciones probabilísticas al problema de la gestión de stocks.

1.4.2. Publicaciones que conforman la tesis doctoral

A continuación se enumeran las publicaciones de la doctoranda que sustentan la tesis doctoral:

1. En "*Stock Management in hospital pharmacy using chance-constrained model predictive control*" (Computers in Biology and Medicine 2016), se realiza una extensión de los artículos de congreso de CDC 2014 y ETFA 2014. Se propone una estrategia consistente en la aplicación de restricciones probabilísticas para los problemas de gestión en este contexto. Esta es la primera publicación de revista de la autora como doctoranda, siendo la quinta autora de un total de siete.

2. En "*An application of economic model predictive control to inventory management in hospitals*" (Control Engineering Practice 2018), se desarrolla un controlador predictivo sencillo y se valida en un entorno real mediante una prueba piloto llevada a cabo con un conjunto de medicamentos de un mismo

laboratorio. En esta publicación la doctoranda es segunda autora detrás de uno de sus directores de tesis.

3. La publicación más reciente es "*A data-based model predictive decision support system for inventory management in hospitals*"[2] (Journal of Biomedical and Health informatics 2020), donde se presentan resultados reales de un sistema de soporte a la toma de decisiones en farmacia hospitalaria basado en datos. Dicho sistema proporciona al farmacéutico diversas alternativas para que este pueda elegir la que sea más oportuna. Cabe destacar que en esta publicación la doctoranda es la primera autora, tratándose además de la primera revista de una de las áreas del JCR.

[2]©2020 IEEE. Este artículo aparece en la tesis impreso con autorización de IEEE y se corresponde con la versión final de: I. Fernandez Garcia, P. Chanfreut, I. Jurado and J. M. Maestre, "A Data-based Model Predictive Decision Support System for Inventory Management in Hospitals," publicado en IEEE Journal of Biomedical and Health Informatics, doi: 10.1109/JBHI.2020.3039692.

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ARTÍCULOS DE REVISTA

Capítulo 2

APLICACIÓN DE CONTROL PREDICTIVO ECONÓMICO A GESTIÓN DE INVENTARIOS EN HOSPITALES

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An application of economic model predictive control to inventory management in hospitals[☆]

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A R T I C L E I N F O

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Model predictive control
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A B S T R A C T

In this paper, we present experimental results from the application of model predictive control (MPC) to inventory management in a real hospital. In particular, the stock levels of ten different drugs that belong to the same laboratory have been controlled by using an MPC policy. The results obtained after four months show that the adopted approach outperforms the method employed by the hospital and reduces both the average stock levels and the work burden of the pharmacy department. This paper also paper presents some practical insights regarding the application of advanced control methods in this context.

1. Introduction

The satisfaction of the clinical needs of a hospital requires the existence of stocked drugs and other materials. Inpatients have a need for medication; doctors use gloves, masks, and tools whenever surgery is carried out; likewise, hospitals also provide specific medicines for external patients, such as those used to treat diseases like AIDS and cancer, which are not supplied in retail pharmacies. These are just a few examples of the hundreds of activities performed in a hospital. To a certain extent, some of these activities are foreseeable. For example, many surgeries are programmed weeks in advance. Others, however, are as unpredictable as accidents and heart attacks. Given the critical nature of the activities performed in a hospital, a certain amount of stocked drugs and materials is necessary to avoid shortages that may have fatal consequences. Hence, inventory management is one of the most important activities carried out in the pharmacy department of a hospital. However, due to the high prices of some of these medicines, whose cost can scale up to hundreds or thousands of euros per unit, this activity also has a substantial impact on the hospital's budget: approximately one-third of the hospital's expenses in goods and services are originated at the pharmacy department (Alvarez & Callejon, 1999).

In this context, operation management is essential to achieve efficiency because it involves planning, organising and supervising the provision of the pharmacy services. An analysis of different quantitative model-based research in operation management is presented in Bertrand and Fransoo (2002). System dynamics is an appropriate approach to study operations management. For example, Größler, Thun, and Milling (2008) shows how system dynamics theory can be very useful to deal with operations management problems. In Mingers and White (2010), the main systems theories and their applications have been considered, including the systems approach, system dynamics, operation research, and so on. Within the operation management area, inventory management is a common need in many businesses and organisations; for example, in supply chains (Cachon, 2001; Çetinkaya & Lee, 2000; Dong, Zhang, & Nagurney, 2004; Kouvelis, Chambers, & Wang, 2006). An optimal management should reduce the average stock levels as far as possible while minimising stockouts. It is necessary to establish a policy that determines when new orders have to be placed while taking into account different types of limitations; for example, uncertainties in demand and delivery times, economic and storage constraints, and the availability of human resources to place orders, receive deliveries, and store goods properly, to name a few. It is needless to say that most stock policies ignore some of these issues for the sake of simplicity. Many of the tasks related to inventory management are still performed manually by staff with only a basic knowledge regarding this matter. For example, the reorder point is one classical approach to this problem, which consists of making an order to have a fixed amount of stocked items whenever the stock is below a certain threshold. This policy is closely related to fixing the amount of items to be ordered,

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whenever the stock is below the threshold. In general, these methods optimise their parameters based on assumptions such as constant delay times and Gaussian distributions for demand. See (Brewer, Button, & Hensher, 2001; Tayur, Ganeshan, & Magazine, 1999) for similar policies.

Given the cross-cutting nature of the problem, in the last few decades many solutions have been proposed to deal with this issue from different areas of research. For example, in Parlar (1988), game theory is applied to an inventory system where two products with random demands are considered. In Axsäter (1993), an inventory system with one warehouse and N retailers is considered. The strategy at the warehouse is similar to an echelon stock, with a periodic review *order-up-to-S* policy. Optimal production control and stock-rationing policies are applied in Ha (1997), where the problem is formulated as a queueing control model. In addition, in the area of control theory, some research related to inventory problems – for example, (Ortega & Lin, 2004)– where the objective is to reduce inventory variation, reduce demand amplification and optimise ordering rules. In this area, the basic approaches can be classified within stochastic control theory and deterministic control theory. Several applications of stochastic control theory to operations research are described in (Neck, 1984). A sliding-mode inventory policy is proposed in Ignaciuk and Bartoszewicz (2010), which also uses stochastic approaches. An implementation of deterministic control theory applied to production–inventory control using frequency domain, was presented by Wikner (1994).

In this article, we work with model predictive control (MPC), which is a successful control method with multiple applications in the industry. MPC uses a mathematical model of the system being controlled to predict its evolution as a function of the sequence of actions implemented during a certain horizon (Camacho & Bordons, 2004). In this way, it is possible to calculate the inputs that optimise a given cost function that penalises any deviation of the expected evolution of the system with respect to the target behavior. From the sequence of actions calculated, only that corresponding to the current time step is actually applied to the system; the rest is discarded and the optimisation is repeated at the next time instant in a receding horizon fashion. As a computer based control approach, it is possible to include issues such as constraints, delays in the problem variables, and disturbances explicitly in the formulation of the optimisation problem. In other words, MPC provides us with a continuous replanning policy that recalculates control actions at each time instant according to the most recent information available that is relevant to the problem being solved, such as unexpected consumption peaks, variation in prices, demand forecast, strikes on the delivery companies, and so on.

In the literature, MPC has been considered on many occasions as a suitable strategy for this type of problem. For example, in Wang, Rivera, Kempft, and Smith (2004) and Wang, Rivera, and Kempf (2005) an MPC policy deals with supply chain management in semiconductor manufacturing. Likewise, in Maestre, Muñoz de la Peña, and Camacho (2011), distributed MPC is applied in simulation to the MIT Beer Game. In Stoica, Arahal, Rivera, and Rodríguez-Ayerbe (2009), robust MPC is used to control a production–inventory system. In Perea-López, Ydstie, and Grossmann (2003), a model predictive control strategy is used to maximise profit in supply chains with multiproduct, multiechelon distribution networks with multiproduct batch plants. In Schwartz, Wang, and Rivera (2006), a simulation-based optimisation is presented to decide, optimally, the internal parameters of internal model control and the model's predictive control policies for inventory management in supply chains under uncertainties are supply and demand. An approach for applying control strategies to inventory management problem in a production–inventory system is presented in Schwartz and Rivera (2010), which uses an internal model control and model predictive control to calculate decision policies for inventory management. In Subramanian, Rawlings, Maravelias, Flores-Cerrillo, and Megan (2013), a distributed model predictive control is proposed to optimise supply chains, particularly cooperative model predictive control. Finally, a variation of MPC is used for the management of inventories and supply chains in Rasku, Rantala, and Koivisto (2004).

In this work, we deal specifically with a recently proposed type of MPC approach; that is, of economic MPC. Under this paradigm, the controller takes the economic objective of the process being controlled as the objective function of the control system (Rawlings, Angeli, & Bates, 2012). Hence, the proposed controller tries to minimise the expenses associated with inventory operations management in the pharmacy department. In particular, we present for the first time real results from a pilot implementation of MPC in a hospital, which was located in *San Juan de Dios* hospital in the Spanish city of Córdoba. In contrast to our previously published works (Jurado, Maestre, Velarde, Ocampo-Martinez, Fernández, Tejera, & del Prado, 2016; Maestre Torreblanca, Velarde, Jurado, Ocampo-Martinez, Fernandez, Isla Tejera, & del Prado Llergo, 2014; Velarde, Maestre Torreblanca, Jurado, Fernandez, Isla Tejera, & del Prado Llergo, 2014), where we carried out simulations to assess several stochastic MPC methods to control inventory levels of individual medicines in a simpler problem setup (e.g., neither storage costs nor storage limits were considered), here we work with all of the drugs belonging to a given laboratory, which is more practical in a real world scenario. Also, to gently introduce this methodology to the pharmacy staff, we designed an MPC strategy that was inspired by the approach followed by the pharmacists to work as a decision support system for them. The controller recommends either placing an order for the drugs or not doing anything. In this very first implementation, we also decided to use the mean consumption of drugs during the last year as the future demand forecast and we aimed to avoid stockouts by means of a safety stock. In this way, the transition towards the implementation of more sophisticated configurations of the MPC will be smoother.

The rest of this paper is structured as follows. In Section 2, the problem setting of inventory management in hospitals is presented. Section 3 describes the formulation of the MPC controller that we implemented. Section 4 presents the results of the application of this controller during four consecutive months and compares these results with historical data from the hospital's database. Finally, Section 5 ends the paper with some concluding remarks and guidance for future work.

2. Problem formulation

This section presents the mathematical model used to build the MPC optimisation problem.

2.1. Pharmacy inventory system

To define a general system, it will be assumed that there are N_i different drugs in the pharmacy inventory. Depending on the demand and the orders, the stock level of each will vary. The stock level evolution for each drug is represented by a discrete linear model, which for the particular case of drug i is

$$s_i(t+1) = s_i(t) + o_i(t-\tau_i) - d_i(t), \tag{1}$$

where $s_i(t) \in \mathbb{Z}$ is the stock of drug i, $o_i(t) \in \mathbb{Z}$ is the number of ordered items of the drug i at time t, considering only one provider, τ_i is its corresponding transport delay, therefore, $o_i(t-\tau_i)$ is the number of ordered items of the drug i at time $t-\tau_i$ and delivered at t, and $d_i(t)$ represents the aggregate demand of drug i.

To differentiate the drugs that need to be ordered from those that do not, a new variable is introduced, $\delta_i(t)$, which is a Boolean variable. If $\delta_i(t) = 1$, then an order for drug i is placed during time t, otherwise $\delta_i(t) = 0$. That way, the number of ordered items can also be represented as $\delta_i(t-\tau_i)o_i(t-\tau_i)$, and $o_i(t) \in \mathbb{Z}$ represents the number of ordered items of drug i, only in those cases where $\delta_i(t) = 1$. This is one of the complicating issues of this type of application because it leads to mixed-integer optimisation problems.

Remark 1. While the time delay in our model is assumed to be constant for the sake of simplicity, in practice it may vary. For example, two orders may b e placed at different moments of time and are delivered on the same day. Some continuous time models do include aggregate states for unfulfilled orders, although they have to average the update rate of the stock to compensate the aggregation (Sterman, 2000). Here, it has been preferred to keep the model as simple as possible and delays are assumed to be constant.

2.2. Optimisation problem

The primary goals of inventory management in hospital pharmacies are: (i) the demand has to be satisfied; (ii) stock levels must be lowered; and (iii) the number of orders placed has to be minimised. Hence, stock levels determine whether to place an order or not and the performance index that we implemented has terms involving demand satisfaction, expenses, and number of orders; that is,

$$\min_{o} J := \beta_1 J_1(o,t) + \beta_2 J_2(o,t) + \beta_3 J_3(o,t), \tag{2}$$

where J_1, J_2 and J_3 are the terms associated with stock levels, orders and expenses, respectively. Weights β_1, β_2 and β_3 prioritise the different terms. The solution of the problem can be substantially changed depending on the values of these weights.

The terms in the objective function (2) are described next in decreasing priority:

(1) J_1: Stock levels. The objective here is to maintain the stock levels as low as possible while satisfying clinical needs. Whenever an order is placed, the calculations are done to guarantee the existence of a safety stock, which is enough to satisfy the maximum demands registered during two days in a row, which is obtained from the hospital's historical data. Hence, once an order is delivered, there is no need to make a new one, at least in the following two days. We used the method presented in Maestre, Isla Tejera, Fernandez, del Prado Llergo, Álamo Cantarero, and Camacho (2012) to calculate the numerical values of these bounds values for the stock. The mathematical condition is expressed as

$$\min_{\delta_i, o_i\ \forall i} \sum_{k=0}^{N} \sum_{i=1}^{N_i} C_{o,i} s_i(t+k), \tag{3}$$

with $s_i(t+k) \geq 0$, where $C_{o,i}$ is the opportunity cost of having drug i in the pharmacy storage, and N is the prediction horizon.

(2) J_2: Expenses. This term of the objective function (2) minimises the expenses in medicines ordered; that is,

$$\min_{\delta_i, o_i\ \forall i} \sum_{k=0}^{N} \sum_{i=1}^{N_i} p_i \delta_i(t+k) o_i(t+k), \tag{4}$$

where p_i is the price for drug i. It is assumed that this is independent on the number of ordered items.

(3) J_3: Orders. With the inclusion of this term in the objective function, the number of orders placed is minimised. This is useful because each request has certain associated costs. This condition is written as

$$\min_{\delta} \sum_{k=0}^{N} \sum_{i=1}^{N_i} C_{op,i} \delta_i(t+k), \tag{5}$$

where $C_{op,i}$ is the cost of ordering drug i. This involves the salary of the pharmacist and the pharmacy assistant during the minutes spent when placing the order and receiving the delivery. Additionally, a shipping cost $C_{sh,i}$ can also be considered as part of this parameter.

As can be seen, each of the three objectives are translated into economic terms. Furthermore, the problem considers the following constraints:

Fig. 1. Unit doses storage room.

Fig. 2. Drug storage shelves.

- **Storage constraints.** Individual constraints arise because each drug may have different storage requirements; for example, unit dose drug boxes (Fig. 1), special shelves with a certain amount of space available (Fig. 2), medical refrigerators (Fig. 3) and so on. Therefore,

$$s_i(t) \in [\mathrm{S}^i_{\min}, \mathrm{S}^i_{\max}]. \tag{6}$$

Note that even though we do not consider here global or group storage limits, they could be imposed if necessary.

Remark 2. Strictly speaking, the stock has to be positive and this is the real hard constraint. In practice, it is common to set a greater bound $\mathrm{S}^i_{\min}(t)$ for safety reasons. The role of this safety stock level is to provide a robustness margin to avoid stockouts in the case of unexpected demands or delays in the deliveries. Nevertheless, violations with respect to this level may occur every now and then without consequences. Hence, there is no need for imposing a strict fulfillment of this constraint in the resolution of the problem.

- **Order constraints.** The formulation of these constraints is done using the definition of the order variable, which is defined by means of two variables: the Boolean $\delta_i(t)$ and $o_i(t)$. If $\delta_i(t) = 1$,

Fig. 3. Medical refrigerator for cold storage.

then an order of drug i is placed during time t. If $\delta_i(t) = 0$, then no order is placed. In case of placing an order ($\delta_i(t) = 1$), $o_i(t)$ represents the number of items ordered. This variable is bounded by both a minimum and a maximum values; that is,

$$o_i(t) \in [O^i_{\min}, O^i_{\max}]. \tag{7}$$

Remark 3. When the Boolean variable $\delta_i(t)$ is used, $O^i_{\min}$ stands for the minimum order size imposed by the corresponding lab. (Distributors do not attend requests if the number of items is too small.) However, without $\delta_i(t)$ it is necessary to introduce non-convex constraints for $o_i(t)$ as

$$o_i(t) \in \{0\} \cup [O^i_{\min}, O^i_{\max}].$$

Again, this is a complicating issue for the optimisation itself. In the next section we show how this problem has been avoided in this work.

In addition, pharmaceutical laboratories do not provide drugs unless a minimum amount of money is spent. That is translated into

$$\sum_{k=0}^{N} \sum_{i=1}^{N_i} p_i \delta_i(t+k) o_i(t+k) \geq O_{\$}, \tag{8}$$

where $O_{\$}$ represents the minimum amount of money to be spent in the order to the laboratory.

Remark 4. Another issue to take into account is that both laboratories and pharmacies have *non-working days* (e.g., Sundays, holidays), which leads to

$$\delta_i(t) = 0, \quad \forall t \in \{\text{working days}\}$$

when the Boolean $\delta_i(t)$ is used. Alternatively, $o_i(t)$ has to be zero in the non-working days.

- **Operational constraints.** These constraints are related to the limited capacity of the pharmacy for placing orders. This fact limits the number of orders placed along the prediction horizon; that is,

$$\sum_{k=0}^{N} \delta_i(t+k) \leq \Delta_i, \tag{9}$$

where Δ_i is the maximum number of orders of drug i that can be placed.

3. Model predictive control

MPC is the methodology that is used here to solve the stock management problem. The basics of this strategy are the computation of a prediction of the system's output over a *prediction horizon* (N) by using a model of the process. An optimisation problem is built upon the predicted trajectory and the control goals to calculate the optimal sequence of inputs during a *control horizon* of length N_u. (After the control horizon, the inputs are assumed to be zero). The first is the control value computed for the current time instant, and it is the only one that is applied to the process: the rest are discarded. This process is repeated at each time instant in a receding horizon fashion.

3.1. MPC setup

This section explains the strategy that we implemented. As will be seen, some modifications were added to make the MPC controller simpler for the pharmacy staff so they could more easily trust the new tool.

Consider the system defined by

$$s(t+1) = s(t) + o(t-\tau) - d(t), \tag{10}$$

where $s(t) = [s_1(t), \ldots, s_{N_i}(t)]$, $d(t) = [d_1(t), \ldots, d_{N_i}(t)]$ and $o(t-\tau) = [o_1(t-\tau), \ldots, o_{N_i}(t-\tau_N)]$, with $o_i(t-\tau) = \delta_i(t-\tau)u_i(t-\tau)$, which represents the number of items of drug i ordered. Note that system (10) aggregates as many instances of (1) as drugs are considered.

The objective is the minimisation of the objective function (2), which represents the pharmacy manager goals. The daily routine of the pharmacy staff involves checking stock levels to guarantee that the levels are high enough to satisfy the clinical needs in the next days (prediction horizon). Otherwise, an order is placed to guarantee that there will be enough medicines. To capture this, we implemented the next algorithm, which consists of the following steps:

1. At the beginning of day k, measure stock levels $s(k)$.
2. If $s(k)$ is enough to guarantee the supply for the hospital needs for N consecutive days with average consumption, then do not order anything and wait for the next day.
3. Otherwise, place an order by solving (2) subject to (6)–(10) and wait for the next day.

Note that the pharmacy staff can force the execution of Step 3 of the algorithm if necessary. Moreover, they can also override the system and make any decision they want in case they are not comfortable with the *suggestion* of the controller. Likewise, it must be noticed that the algorithm is *executed* asynchronously due to the non-working days; for example, no orders are placed during the weekends.

3.2. Implementation

The MPC that results from the direct implementation of the inventory management problem presents some challenging features, such as non-convex constraints and integer optimisation variables. For this reason, we exploited some properties of the problem to reduce its complexity:

- In the first place, the minimum bound for an order of drug i, $O^i_{\min}$, can be assumed to be 0 once it has been decided that an order is going to be placed to the laboratory. In particular, the need for $O^i_{\min}$ stems from the minimum budget required by the laboratory $O_\$$; that is, $O^i_{\min}$ units are enough to satisfy the minimum budget constraint imposed by $O_\$$ when the drug is considered *individually*. Hence, these are redundant constraints and we just take $O^i_{\min} = 0$ once it is known that an order will be placed.
- Once it has been decided to place an order for one drug, then there is really no need to consider the binary variables of the rest of the drugs because they all belong to the same laboratory. By assuming an aggregate cost for placing an order, we can consider only one binary variable $\hat{\delta}(t)$ at time step t, so that $\delta(i) = \hat{\delta}(t)$ for any drug i that belongs to the laboratory used in the experiments. Consequently, the number of binary variables becomes simply N_u, which considerably reduces the computation burden of the problem.
- States and orders are relaxed to have a continuous optimisation problem in these variables, which generates a mixed integer linear program. There are specific techniques to solve this problem (e.g., branch and bound (Lawler & Wood, 1966), genetic algorithms (Summanwara, Jayaramana, Kulkarnia, Kusumakarb, Guptab, & Rajesh, 2002) and the cutting-plane method (Cook, Kannan, & Schrijver, 1990)) but, given the low number of binary variables, we have performed an exhaustive search on them to compute the solution.
- The solution of the problem is rounded up to have a number of boxes since drugs are generally not sold in units. Note that the rounding procedure guarantees the availability of drugs for the prediction horizon but it generates sub-optimality in the solution. For example, if only one drug is required, then it may be necessary to complete the order with others. There are many feasible options to solve this issue and in principle there is no guarantee that the choice made by the controller is optimal.
- Finally, we considered here $N_u = 1$, which captures the mental process of the pharmacy staff by analyzing *whether* an order should be placed at the current time step. Simulations with larger control horizons are also included to assess the effect of the N_u on performance.

Remark 5. Orders are calculated to make stock levels greater than the bound values used in the optimisation along the horizon (as long as the demand behaves as expected). However, checking step 2 focuses only on avoiding this problem during the next N days. Hence, the bound levels become a sort of replenishment references when the order is calculated and stock levels can be below them. In other words, the controller makes its calculations to guarantee that an average demand can be satisfied during the whole prediction horizon without violating the safety bounds; otherwise an order is placed. Note also that the safety stock is enough to guarantee the satisfaction of clinical needs of the hospital in the worst 48 h scenario recorded during the last year according to the hospital data, which is a rather conservative assumption. Finally, if a stockout occurs, then a drug loan can be asked from one of the neighboring hospitals, which mitigates the consequences derived from such an event.

4. Case study and results

In this section, we present the results obtained from the application of the MPC policy to manage the inventory levels of a group of ten drugs provided by the same laboratory, considering that all management goals are equally relevant; that is, $\beta_1 = \beta_2 = \beta_3 = 1$. The test was performed in San Juan de Dios hospital, which is located in the Spanish city of Córdoba, during the four-month period from 2 September 2016 to 3 January 2017. It must be noted that it is not possible to provide the real names of the drugs here for the sake of confidentiality.

Table 1
Stock safety levels for two days without new orders being delivered, unit price, and units per box.

		Safety level			Prices/unit	Units/box
		1	0.99	0.98		
med #	1	573	531	440	0.47	10
	2	205	135	100	0.71	5
	3	50	40	30	2.91	10
	4	50	30	30	1.87	10
	5	7	6	5	31.44	4
	6	14	7	5	37.09	4
	7	12	10	7	1.49	10
	8	12	10	7	1.45	10
	9	13	9	7	1.25	20
	10	124	74	68	0.15	50

Before the test period, the hospital provided historical data regarding stock levels, demands and orders of the medicines considered corresponding to the period 1 September 2015 to 1 September 2016. The information was analyzed to generate bound levels for the controller. Table 1 shows the stock needed for each item to attain a certain safety level during two consecutive days with no orders delivered. For example, if the stock for drug #1 is 573 and the demand behaves as in the historical data, then it would be possible to avoid stockouts during two days with a 100% guarantee. A lower stock implies assuming a certain risk for this drug according to the data. Here, we used the 100% safety level as a lower bound for the stock during the horizon, which usually corresponds to 10–15 days of average consumption for most medicines. More information regarding the construction and use of this type of table in hospital pharmacy is provided in Maestre et al. (2012). Note that the use of a safety stock is a very common practice in this context and was also previously used by the pharmacy department. In addition, given that it is based on empirical data, a certain connection can be established with Jurado et al. (2016), where chance constraints are calculated by using this type of information. It should also, be noted that Table 1 provides information regarding the price of the drugs under study and the number of units in each box.

The management method of the hospital before the application of the MPC consists of a reorder point policy. More specifically, orders are placed whenever the stock of a certain drug is below a certain threshold. If the amount to be ordered is enough to satisfy the minimum budget of the laboratory, the then order is placed. Otherwise, the pharmacists look at other items provided by the same laboratory to complete the order. Nevertheless, additional factors are taken into account by the pharmacy staff that can modify the strict application of the reorder point method, such as offers, coming holidays and the number of inpatients using a certain drug.

Given that it was the first implementation of MPC in the hospital, we decided to use the same demand forecast used by the pharmacy staff, which is very simple: the expected daily demand is its average value calculated during the last year. With this forecast, the horizon of the controller N was set to 12 days by using a simulation based trial and error approach. This result is also coherent with the aforementioned choice of the safety levels. Hence, the policy of the controller can be described as follows: if the constraints of the problem can be satisfied by the expected evolution of the stock levels with no items being delivered during the next 12 days, then the controller suggests not to place a new order; otherwise, an optimal order is calculated for the drugs under study. Acquisition costs are set by prices and storage costs are calculated as the opportunity cost of the money invested on stocked items. The other costs that are considered by the controller are based on information provided by the pharmacy staff regarding average times of placing orders, salary, and so on.

The evolution of the stock levels and the orders placed during the test period are shown in Fig. 4. As can be seen, the fact that all drugs have

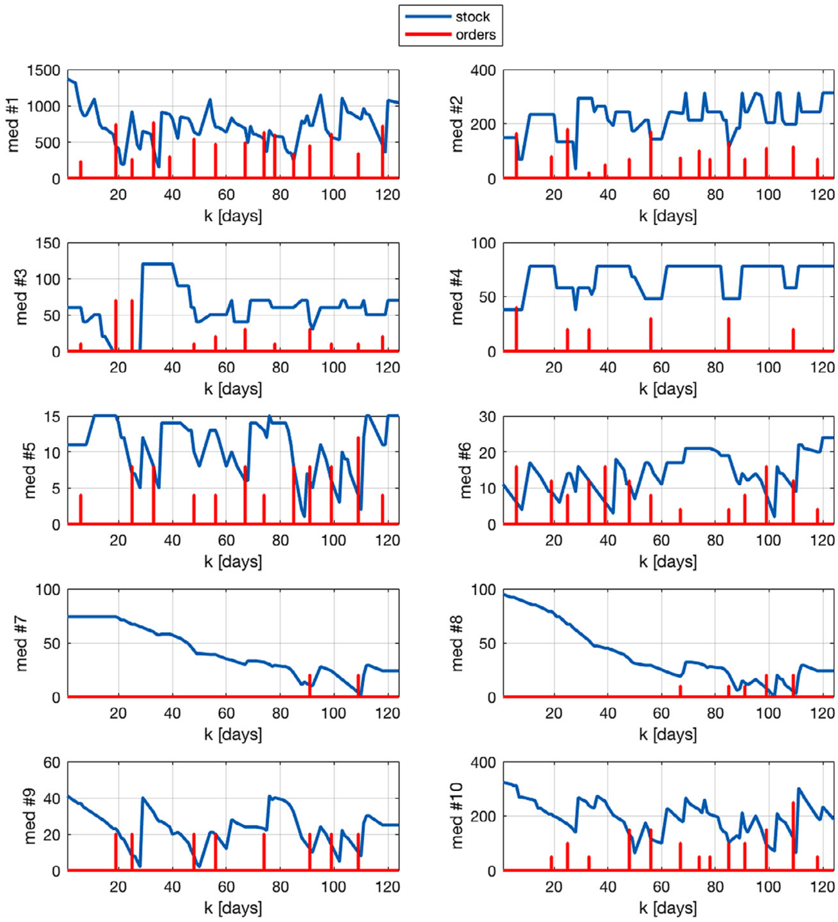

Fig. 4. Evolution of stocks during the test period.

the same provider allows us to group the requests to save costs and also to satisfy the minimum budget constraint imposed by the laboratory. These results are analyzed by means of the following key performance indicators (KPI), which have been computed to highlight and quantify the differences with respect to the previous policy used by the hospital:

- Mean value (μ_i): the importance of this value goes beyond its meaning as a statistic. The mean value of drug i allows us to quantify the average amount of money invested on this medication.
- Standard deviation (σ_i): the standard deviation of drug i provides us with information regarding the fluctuations of stock levels.
- Maximum (M_i): maximum number of items stocked in the period of study.
- Minimum (m_i): minimum number of items stocked in the period of study.
- Number of stockouts (SO_i): stockouts registered for drug i in the period of study.
- Order rate (OR_i): number of days where an order for drug i was placed divided by the days of the period of study. This KPI is important because it is closely related to the activity of the pharmacy department.
- Average order (AO_i): number of items ordered on average when an order for drug i was placed during the period of study.

The results regarding these KPI are shown in Table 2. In general, most drugs improve their average, standard deviation, and maximum values. The minima indicate that there was no shortage of medicines during the MPC period, although it was close for medicines #3 and #8 because there was no stock in certain moments. The order rate seems to be worse with our approach because more orders are placed when this parameter is examined individually. Consequently, the average order size drops. However, from a global perspective, the order rate was also reduced. During the previous year, 31% of days an order was placed to the laboratory. During the test period, the order rate dropped to 12.5%. This happened because the MPC policy groups orders; that is, once a request is made to the laboratory, several drugs are ordered together at the same time, which saves both money and time.

Table 2 also shows an assessment of the MPC implemented with respect to versions with longer control horizon. In particular, the initial state and the demand obtained during the test period were used to test MPC controllers with $N_u \in \{3, 5, 7, 9\}$. As it turns out, the controller becomes less conservative with these control horizons because it considers several order points in the horizon. Consequently, stock levels are lower on average but this has a cost in terms of stockouts. Nevertheless, we must remark that the simulations were carried out at the same value for the rest of the parameters that define the controller; that is, we studied changes on N_u *ceteris paribus*. Had any of these controllers been implemented, then we should have tuned all the parameters carefully by using the data provided by the hospital.

Fig. 5 shows a comparison between the results with the previous hospital policy and the MPC based ones. The boxplots are drawn following the usual standards: a box is plot for each drug, where the central red mark is the median and the lower and upper edges represent, respectively, the 25th and 75th percentiles. In addition, whiskers are extended to the most extreme values not considered as outliers.[1] Finally,

[1] Points are depicted as outliers when they are outside the range $[Q_1 - 1.5 \cdot (Q_3 - Q_1), Q_3 + 1.5 \cdot (Q_3 - Q_1)]$, where Q_1 and Q_3 are, respectively, the 25th and 75th percentiles.

Table 2
KPI based comparison between the previous hospital policy, the MPC implemented in the experiment, and other versions of the controller tested via simulation with longer control horizon.

		μ_i	σ_i	M_i	m_i	SO_i	OR_i	AO_i	μ_i	σ_i	M_i	m_i	SO_i	OR_i	AO_i
		Sep 1st, 2015–Sep 1st, 2016							Sep 2nd, 2016–Jan 3rd, 2017 (Real MPC $N_u = 1$)						
med #	1	1282.81	604.95	2387	−1	1	0.07	748.07	741.07	256.67	1365	150	0	0.20	480.62
	2	217.40	98.41	447	−7	6	0.06	129.56	224.65	62.59	314	34	0	0.18	98.33
	3	37.38	20.17	98	−2	9	0.04	34.61	58.54	30.21	120	0	0	0.13	26.36
	4	57.90	20.83	100	0	0	0.05	32.50	67.99	14.37	78	38	0	0.07	26.66
	5	12.07	5.97	27	0	0	0.09	6.36	10.78	3.71	15.00	1	0	0.16	6.46
	6	22.77	6.19	37	9	0	0.07	7.64	14.44	5.57	24.00	2	0	0.16	10.15
	7	59.92	16.97	96	27	0	0.08	10.60	40.35	21.98	74.00	2	0	0.02	20.00
	8	62.06	20.83	118	22	0	0.08	11.50	38.15	26.36	95.00	0	0	0.07	13.33
	9	49.31	18.13	86	6	0	0.07	12.20	23.18	9.90	41.00	2	0	0.11	20.00
	10	202.39	92.65	516	14	0	0.09	106.35	192.53	61.89	323	64	0	0.17	110.71
		Sep 2nd, 2016–Jan 3rd, 2017 (Sim. MPC $N_u = 3$)							Sep 2nd, 2016–Jan 3rd, 2017 (Sim. MPC $N_u = 5$)						
med #	1	410.22	272.29	1365	−7	1	0.41	214.71	414.92	274.48	1365	−8	1	0.41	213.82
	2	156.08	53.92	269	44	0	0.35	49.31	157.58	50.31	269	64	0	0.35	48.79
	3	55.38	32.76	130	−10	2	0.20	18.12	62.31	33.06	130	−10	2	0.22	16.67
	4	58.61	12.83	78	38	0	0.20	10.62	63.26	19.26	98	28	0	0.21	11.18
	5	8.89	4.53	18	−5	5	0.22	4.44	8.52	3.63	14	−2	4	0.22	4.44
	6	12.15	5.68	21	0	0	0.28	5.74	12.51	5.93	23	−3	2	0.29	5.50
	7	47.73	20.18	74	4	0	0.07	10.00	80.88	11.05	104	60	0	0.16	10.00
	8	43.29	26.40	95	0	0	0.11	10.00	70.02	11.13	95	49	0	0.16	10.00
	9	27.82	12.96	52	−12	3	0.12	20.00	60.51	32.41	125	−12	1	0.17	20.00
	10	145.98	78.01	323	9	0	0.29	58.33	139.63	79.58	323	9	0	0.28	60.87
		Sep 2nd, 2016–Jan 3rd, 2017 (Sim. MPC $N_u = 7$)							Sep 2nd, 2016–Jan 3rd, 2017 (Sim. MPC $N_u = 9$)						
med #	1	411.68	274.78	1365	−8	1	0.40	220.30	409.99	275.40	1365	−8	1	0.41	213.82
	2	156.96	50.61	269	64	0	0.34	50.54	156.19	50.36	269	64	0	0.35	48.79
	3	62.54	34.13	140	−10	2	0.23	15.26	59.15	34.07	140	−10	2	0.21	17.06
	4	59.65	12.31	78	38	0	0.18	10.67	58.11	12.09	78.00	38	0	0.18	10.67
	5	8.73	3.68	16.00	−1	1	0.24	4.00	8.61	3.75	16	−1	1	0.24	4.00
	6	12.05	6.42	25	−2	2	0.28	5.74	12.54	6.56	25	−2	2	0.27	5.82
	7	93.27	13.50	117	67	0	0.16	10.00	86.50	9.99	107	67	0	0.15	10.00
	8	82.40	10.16	106	61	0	0.16	10.00	75.63	10.92	96	51	0	0.15	10.00
	9	85.28	39.56	137	−12	1	0.17	20.00	71.74	31.63	117	−12	1	0.16	20.00
	10	149.82	82.70	323	−29	2	0.28	60.87	145.59	81.15	323	−29	2	0.28	60.87

Table 3
Overall results for the experiment period for the hospital (estimated), the implemented MPC and the assessed MPC via simulation.

	Real		Simulated MPC			
	Hospital	$N_u = 1$	$N_u = 3$	$N_u = 5$	$N_u = 7$	$N_u = 9$
#Orders	41	16	35	35	34	35
Savings (€)	–	644.89	977.43	829.05	761.91	796.39
#Stockouts	6	0	11	10	8	9

Table 4
KPI of the previous hospital policy in the same period, one year before.

		μ_i	σ_i	M_i	m_i	SO_i	OR_i	AO_i
		Sep 2nd, 2015–Jan 3rd, 2016						
med #	1	557.19	341.93	1378	−1	1	0.10	608.33
	2	222.67	111.91	447	−7	6	0.07	133.75
	3	24.33	23.12	98	−2	9	0.04	32.00
	4	62.65	19.76	100	10	0	0.06	31.43
	5	11.02	7.51	25	0	0	0.11	6.62
	6	20.22	4.66	33	9	0	0.06	6.57
	7	58.83	18.37	96	27	0	0.08	9.30
	8	65.39	13.89	91	42	0	0.08	7.30
	9	57.44	14.21	73	24	0	0.07	5.88
	10	154.93	67.86	276	14	0	0.08	87.50

the outliers are plotted individually. This allows us to compare at a glance the results from the policy of the hospital and those of MPC.

Finally, from an economic viewpoint, the hospital was able to free 644.89 euros by lowering its average stock levels in this group of drugs thanks to the implementation of the controller; that is, part of the average inventory expenditures could be retrieved. Note that the savings derived from the stocking costs are not included in this amount; that is, it represents average savings on items. In addition, it is estimated that the hospital would have placed 25 extra orders to the lab during the four month period. Interestingly, these results were obtained without stockouts, which proves that the choice of the parameters of the controller (e.g., prediction and control horizon and safety levels) was appropriate. Table 3 summarises these results and also extends the comparison to the simulated MPC with longer control horizon. As can be seen, the simulated controllers provide greater savings by increasing the number of orders and the number of stockouts. Nevertheless, these results suggests that there is room for improvement in future experiments by choosing longer horizons.

Remark 6. We used twelve months and not four to assess the hospital policy due to several reasons: (i) the activity of the pharmacy depends on the period of the year; for example, Spanish people go on holidays either in July or August; (ii) in some periods of the year, there can be special offers placed by the laboratories that have an meaningful effect on the stock; and (iii) the accuracy of the information systems in the hospital is not perfect; that is, stock levels and orders were not as controlled as in the experiment period. For all these reasons, we preferred to use average results of a longer period for the hospital.

Nevertheless, the reader may wonder how the results would look like if the comparison were established using results obtained by the hospital policy in the same period during the previous year. These additional results are presented in Table 4. In this period, the hospital placed 40 orders and had 16 stockouts, which concentrated in the first three drugs. Even when the average levels of the hospital were lower for some drugs, the MPC policy also outperforms the hospital policy here, saving 158 euros.

5. Conclusions

We have presented results from the application of an economic MPC policy to control inventory levels in the pharmacy department of a

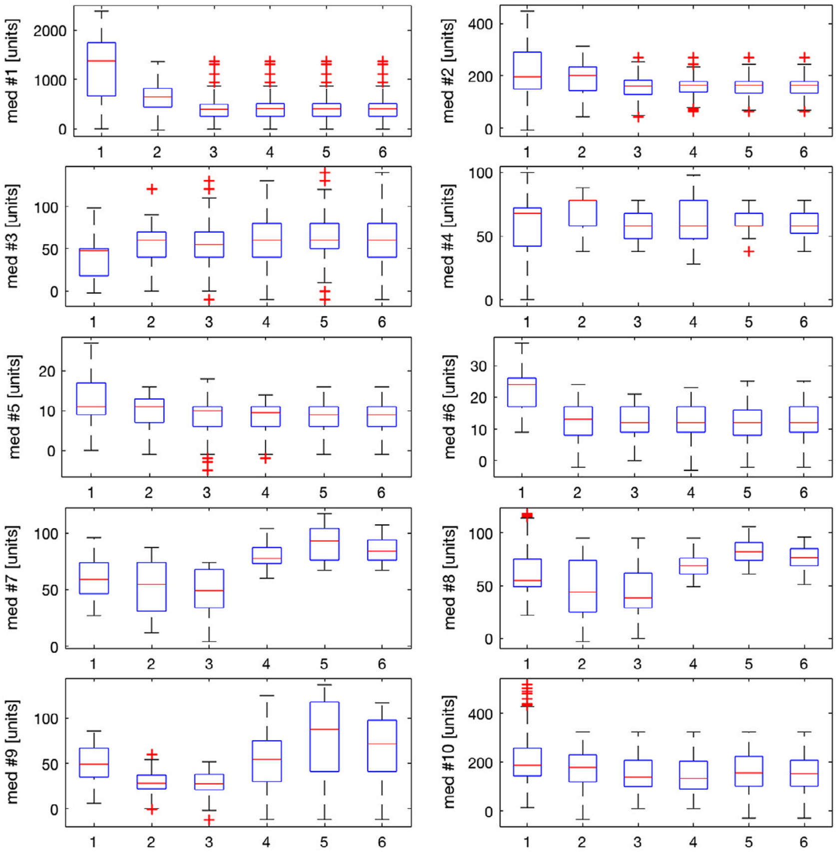

Fig. 5. Boxplot results comparing results of the hospital policy (1), the implemented MPC policy (2), and the simulated MPC controllers with $N_u = 3$ (3), $N_u = 5$ (4), $N_u = 7$ (5), and $N_u = 9$ (6).

medium size hospital located in Spain. Our results show that, even with a conservative and simple formulation of the controller, it is possible to outperform the policy of the hospital. For this reason, we believe that there is room to improve on these results by more aggressively tuning the controller (at least for some medicines) and exploiting the recent bloom on stochastic MPC formulations, some of which have even been tested in simulation in a simplified version of this problem (Jurado et al., 2016). In addition, the simulations performed with longer control horizons offer better economic results but at the cost of more stockouts. There is a trade-off between conservativeness and economic savings that is determined by the choice of the parameters of the controller. Simulations based on the data from the information systems of the hospital are essential to find the best tuning.

Nevertheless, some comments regarding the accuracy of the information systems of the hospital are in order. The staff working in the pharmacy are usually saturated with the amount of work that they have. In fact, it is not rare that the workforce is occasionally enhanced by temporary contracts. During the peak periods of work, the databases may be updated later than they should be; for example, an order is delivered and the drugs are available (and possibly used) but this is only included in the information system following a certain delay (even days in the worst cases). There are other common disturbing issues. For example, a member of staff forgets to reflect in the information system that a certain drug was taken, an event that generates errors in the information. Consequently, there is a need for stocked items to be counted several times a year so that these errors can be detected and corrected. In addition, drugs may be returned from the departments at the hospital, which usually have a small stock of items themselves. This is translated into negative demands that increase the pharmacy's stock unexpectedly. During the experiment period, we would speak daily with the pharmacy staff to see how the stock was evolving and avoid problems in the information handled by the controller. However, it is clear that the design of software for stock management in this context should take into account the uncertainty generated by these events.

Our experience has also taught us that the implementation of this type of techniques requires the pharmacy staff to be trained so they can place trust in methods that are novel for them. The tools are programmed provide them with a decision support system that they can overrule at will, and it takes some time before they feel completely comfortable with the lower average inventory levels. Discussions regarding the placement of new orders when the controller was recommending not to do anything emerged in different moments of the test period. In the end, the controller was only forced to calculate a new order on one occasion, and the results showed that following the advice of the program would not have led to stockout. Hence, it is necessary to train the pharmacy staff but also to tune the system to a risk level that they can feel comfortable with.

Another noteworthy point is that the simplicity of the problem can be deceiving. Even when the system dynamics can be modeled by means of integrators and delays, reality is more complex. As we just saw, issues may arise regarding the accuracy of the hospital's information systems. In addition, delivery delays are not constant and prices can change from time to time due to the offers made by laboratories. There may even be need to change the constraints of the problem; for example, when a refrigerator is broken or when some drugs are offered so cheaply that it can be preferable to allow extra space for stocking. In this dynamical problem setup, the role of the pharmacist is essential to take advantage of the receding horizon nature of the MPC controller because the problem can be updated with the most recent information available in a flexible manner. For example, if two different orders happen to be delivered on the same day, then the stock is simply updated with the items received and the calculations are repeated without these pending deliveries. Without this *cooperation*, the orders calculated by the controller will not be completely accurate and a certain trend to overrule the controller can emerge. Hence, the interface between the controller and the pharmacists has to be very carefully designed to maximise the usability and usage of the software.

After looking into our results, we can conclude that the fact that the implemented controller was using $N_u = 1$ increased the conservativeness of the solution and also helped to avoid stockouts. The simulations show that longer horizons relaxed the policy of the controller and they would have required a different choice for the other parameters. In addition, it has been beneficial to consider joint orders for all of the medicines that belong to the laboratory. Orders are placed in a smarter way because they are completed based on the controller and not on the decisions of the staff, which was the case whenever the reorder point of one of the drugs required an order to be placed.

Finally, we expect to test more advanced formulations of the controller in the future, also taking into account the lessons learned during this test. In particular, we plan to explore ways of implementing the policy based on integer programming; that is, looking for the optimum of the problem and not an approximation provided by the relaxations performed.

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Capítulo 3

SISTEMA PREDICTIVO DE SOPORTE A LA DECISIÓN BASADO EN DATOS PARA LA GESTIÓN DE INVENTARIOS EN HOSPITALES

A Data-based Model Predictive Decision Support System for Inventory Management in Hospitals

Isabel Fernández, Paula Chanfreut, Isabel Jurado and José María Maestre

***Abstract*—This paper presents experimental results from the application of a data-based model predictive decision support system to drug inventory management in the pharmacy of a mid-size hospital in Spain. The underlying objective is to improve the efficiency of their inventory policy by exploiting pharmacy historical data. To this end, the pharmacy staff was aided by a decision support system that provided them with quantities needed for the satisfaction of clinical needs and the risk of stockout in case no order is placed for different time horizons. With this information in mind, the pharmacy service takes the final order decisions. The results obtained during a test period of four months are provided and compared with those of a previous model predictive control approach, which was implemented in the same hospital in the past, and with the usual policy of the pharmacy department.**

***Index Terms*—Hospital pharmacy, Inventory management, Data-based decision support system**

I. Introduction

THE acquisition and storage of the medicines necessary to cover the clinical activities of a hospital are some of the primary management tasks performed by a Hospital Pharmacy Service. The societal relevance of the clinical needs and the frequent urgent requests coming from the rest of the hospital services (e.g., for inpatients, consultations, operating rooms, day hospital, outpatients, etc.) make extremely important to control the stock robustly so that stockouts are avoided, and the satisfaction of the demand can be guaranteed. Unfortunately, the high costs of many drugs –some items may cost several hundred or even thousands euros per unit– generates a substantial impact on the hospital budget, which is usually very constrained. Also, the staff working in the Pharmacy Service is limited, thus bounding the number of orders that can be placed and receptioned every day. As a result, a trade-off between demand satisfaction, inventory-related costs, and work burden must be attained, which requires to control the size of the orders and their frequency carefully and to avoid, as much as possible, expiration and unnecessary immobilization of resources. In addition, this problem also presents additional constraints and complicating issues. For example, it is important to take into account the space requirements for storage, especially for those that require refrigeration, given that the refrigerated storage rooms have much more restricted space and thermolabile medicines are becoming more numerous (in addition to the classic ones such as insulin, certain cytostatics, and the novel monoclonal antibodies). Likewise, orders may suffer transport delays and weekends and other holidays of the hospitals, labs, and distributors may impose additional constraints regarding order placement and delivery reception.

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In short, on the one hand, clinical needs must always be satisfied. However, the limitations of financial resources and logistical constraints require the use of acquisition strategies that minimize the amount of product to be stored, assuring, with a certain degree of certainty, that they respond to the clinical demand for a certain period [1], [2]. Hence, the relevance of applying a good management policy that meets these conflicting objectives. The implementation of efficient stock management strategies can lead to significant economic savings [3], [4], taking into account that up to 35% of purchases in goods and services in a hospital come from the Pharmacy Service [5], [6].

In general, stock management techniques are widely used in different businesses and organizations in order to optimize the use of resources, as the immobilized money due to the stock. With that objective, there are several common policies that decide when and how to place new orders [7], [8], [9]:

(1) A classic and very used approach is that of the reorder point (s, S), which consists of placing a new order to have S stocked items whenever the stock is below s. This strategy implies that the amount of items to order is almost fixed. These types of methods make different assumptions, e.g., constant transport delays and Gaussian distributions for the demand [10], [11]. For example, in [12], an (s, S) inventory optimization problem is solved and applied in a case study of a hospital in Turkey.

(2) The inventory policy (R, S) is applied in [13] for supply chains with four echelons. They consist of a manufacturing plant, a vendor distribution center, a retailer distribution center, and a retailer out-let store. This strategy assumes that R is the review interval, and S is the order-up-to-level. Also, demand and lead times are assumed to be stochastic variables in the model.

A noteworthy point is that stock does not need to be *locally* controlled. Indeed, in vendor-managed inventory policies vendors monitor their customers' stock, place orders and trigger deliveries. Following this idea, some works study the supply chain parameters and their effect on cost savings assuming a deterministic demand [14].

In general, simpler management policies are based on simplifications that result in a loss of performance. For example, since non-stationary policies increase the complexity of the problem, many studies consider time-varying deterministic

Fig. 1. Pharmacy Service at San Juan de Dios hospital in Spain. Monodose area.

demands, which is not realistic. Indeed, the costs of assuming a stationary demand are studied in [15]. Some works that deal with this problem are: [16], where an integer linear programming model for inventory lot-sizing and supplier selection problem is presented; [17], which models the non-stationary and stochastic demand by means a Markovian representation, also accounting for computation complexity and cost effectiveness of the policies; in [18], the demand is non-stationary over a finite set of periods and the inventory policy follows the FIFO strategy (first in, first out); a data-driven approach to model stock levels is presented in [19], which works with time-correlated and non-stationary demand; and [20], which develops a stochastic inventory model which combines FIFO and LIFO (Last In, First Out) policies under a non-stationary random demand.

Typically, model misspecifications and information losses derived from simplifying assumptions are mitigated by setting a safety stock to minimize stockouts at the expense of raising average inventory levels. Likewise, the safety stock also helps these methods deal with unexpected realizations of the demand and also with the different sampling times used for stock management in order to achieve a feasible work burden for the staff. In particular, Pareto principle is often applied in this context. As can be seen in Figure 1, the pharmacy department deals with hundreds of different products. For this reason, items are partitioned in several groups depending on their economic impact. In this way, the most expensive items are more frequently ordered than the inexpensive ones, leading to lower and higher average inventory levels, respectively.

Nowadays, with the new technologies and the growing amount of information available due to the pervasive presence of computation is easier to use more sophisticated techniques for supply chain and inventory management problems. For example, in [21], [22], [23], [17], the inventory management problem is formulated in a Markovian decision process framework assuming stochastic demands. Recently, data-driven approaches are also gaining relevance, as shown in [24], [25], where different techniques and algorithms are reviewed, and [26], [27], which provide supporting arguments regarding the impact of data science and predictive analytics in supply chain management. Also, a data-driven approach that considers time-correlated and non-stationary demands is proposed in [19]. Likewise, the abundance of data can be directly exploited by methods such as model predictive control (MPC), which optimizes the sequence of future actions and states of a system along a given horizon while explicitly considering constraints on system variables and the uncertainty in exogenous inputs as the demand. An application of data-based stochastic MPC for this type of application can be found for example in [28], [29], where historical data were used to simulate a chance-constrained MPC.

The work presented in this article uses a different stochastic MPC strategy, namely, scenario-based MPC [30], [31], so that multiple previous realizations of the pharmacy demand are used in the computations. In particular, stochastic MPC is the core of a decision support system that presents order placement *suggestions* and assesses risks. Hence, a significant difference with other works in the literature is that the controller does not implement the actions computed. Instead, it is the pharmacist who chooses among the possibilities presented by the decision support system, which runs the data-based MPC policy for different horizons and risk levels. Hence, the orders finally implemented benefit from both the scenario-based MPC controller and the pharmacist knowledge. In this regard, this work aligns with other human-in-the-loop control methods such as [32] and, especially, [33], where operator selects actions within a set provided by the control system.

The proposed data-based decision support system is actually applied to the pharmacy of the hospital *San Juan de Dios* in Córdoba, Spain. The results obtained along a four month test period are assessed via simulation with a previous MPC controller implemented in the pharmacy [34] and a perfect forecast MPC. Likewise, the comparison is complemented with the results of the actual policy followed by the hospital when these controllers are not operating.

Finally, this work is embedded into a project named *Pharmacontrol*, where different hospitals in Andalusia cooperate with the Higher Technical School of Engineering of the University of Seville to assess and implement new strategies that improve the efficiency of Hospital Pharmacy Services. Before this project, the management policy used was based mainly on the previously mentioned technique of the reorder point. Nevertheless, the pharmacy staff used that only as a reference because other factors are also considered when placing a new order, e.g., fluctuations of the demand, the number of patients under treatment with highly controlled medicines, the proximity of the end of week and holidays in which orders are not served, and the need of other drugs from the same provider to reach the minimum amount established to place an order.

The remainder of the article is structured as follows: Section II presents the problem formulation. Section III explains the proposed methodology to improve the hospital drug inventory management policy. Section IV shows the experimental results obtained. Finally, conclusions are drawn in Section V.

Fig. 2. Hospital pharmacy storage area.

II. Problem Statement

The objective is to use historical pharmacy inventory records to support decisions regarding the size and timing of new orders. To this end, we consider a rolling horizon approach in which suggestions for inventory decisions are generated considering previous realizations of the demand to predict the stock evolution in the following days. The elements leading to the corresponding optimization problem are introduced in the next subsections, namely, the model describing the pharmacy inventory system, its constraints, and the main goals of the pharmacy service.

A. Pharmacy Inventory System

The hospital pharmacy manages a set $\mathcal{M} = \{1, 2, \ldots, M\}$ of medicines (hereinafter also referred to as *meds*) with time-varying inventory levels due to the deliveries coming from a set $\mathcal{P} = \{1, 2, \ldots, P\}$ of pharmacy distributors and the uncertainty of the demand from the different hospital services.

Let $s_i(t) \in \mathbb{Z}_{\geq 0}$ and $d_i(t) \in \mathbb{Z}$ respectively be the stock and demand of drug $i \in \mathcal{M}$ at day t, and $o_i^j(t - \tau_i^j) \in \mathbb{Z}_{\geq 0}$ represent the units of drug i ordered to provider $j \in \mathcal{P}$ τ_i^j days ago, with τ_i^j representing the transport delay.[1] Thus,

$$r_i(t) = \sum_{j \in \mathcal{P}} o_i^j(t - \tau_i^j). \tag{1}$$

units of drug i are received at day t, whereas

$$o_i(t) = \sum_{j \in \mathcal{P}} o_i^j(t) \tag{2}$$

represents the units of drug i ordered at day t. Given the demand, and the corresponding drug deliveries, the following discrete-time linear model can be used to represent the evolution of stock of drug i

$$s_i(t+1) = s_i(t) + r_i(t) - d_i(t), \tag{3}$$

from where it is clear that any constraint on the stock becomes stochastic due to the uncertainty of the demand.

[1]While the stock and the orders are integers greater or equal than 0, the demand can occasionally be *negative* due to items returned to the pharmacy.

Fig. 3. Hospital pharmacy storage refrigerator.

B. Pharmacy Constraints

In order to obtain valid results, it is necessary to take into account the following constraints:

(i) **Storage constraints.** The storage space in the pharmacy is limited as can be seen in Figure 2, very particularly R2.4.
for cold storage drugs, which are shown in Figure 3. Thus, the stock levels should remain below admissible values, especially for those drugs that must be stored in refrigerators. Likewise, stocks are required to be either 0 or positive. These constraints are translated into a minimum 0 and maximum number $\mathrm{s}_i^{\max}$ of units for each drug $i \in \mathcal{M}$, i.e.,

$$s_i(t) \in [0, \mathrm{s}_i^{\max}]. \tag{4}$$

Note that the minimum could also be imposed by the safety stock, in case it is used.

(ii) **Order placement constraints.** The number of units ordered for each med $i \in \mathcal{M}$ can either be zero or be bounded by a minimum and a maximum value, i.e.,

$$o_i(t) \in \{0\} \cup [\mathrm{o}_i^{\min}, \mathrm{o}_i^{\max}]. \tag{5}$$

Since this constraint set is not convex, a binary variable $\delta_i(t)$ modeling the action of order placement can be introduced to deal with this issue. In this way, $\delta_i(t) o_i(t)$ represents the number of ordered units, so that $o_i(t) \in [\mathrm{o}_i^{\min}, \mathrm{o}_i^{\max}]$ iff $\delta_i(t) = 1$.

Also, pharmaceutical laboratories do not provide drugs unless a minimum amount of money is spent. This constraint can be posed as

$$\sum_{i \in \mathcal{M}} c_i^j o_i^j(t) \geq \mathrm{o}_{\$}^j, \tag{6}$$

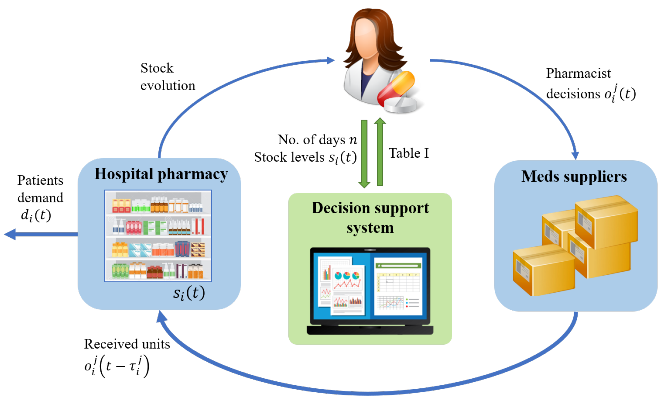

Fig. 4. Steps and components of the proposed DB-MPDSS: 1) at the beginning of day t, the pharmacist observes the stock levels of each med; 2) this information is introduced into the MPDSS, together with the desired value(s) for n (from 2 to 8 in the performed test); 3) the DB-MPDSS processes the data and provides the pharmacist with Table I and the orders for each case considered; 4) the pharmacist evaluates this information and places the corresponding orders; 5) meds arrive to the pharmacy after the corresponding transport delay.

where $o_\$^j$ represents the minimum amount of money to be spent when placing an order to supplier $j \in \mathcal{P}$ and c_i^j is the unitary cost of drug i.

(iii) **Non-working days.** Another issue to take into account is that labs, distributors, and pharmacies have *non-working days* (e.g., Sundays, holidays), which leads to

$$o_i(t) = 0, \quad \forall t \notin \{\text{working days}\} \tag{7}$$

(iv) **Work burden.** Due to the limited staff at the pharmacy, a constraint has to be imposed on the orders that can be daily handled, which also limits the corresponding deliveries, leading to

$$\sum_{i \in \mathcal{M}} \delta_i(t) \leq \delta_{\max}. \tag{8}$$

C. Goals of the Hospital Pharmacy Service

Given the critical nature of the application we deal with, the primary concern is to ensure that the required meds are available at all times to the patients. Nevertheless, a further objective is to increase inventory efficiency by reducing ordering and holding inventory expenses, i.e., lowering the number of orders placed and stock levels. From an MPC viewpoint, at day t, the pharmacy managers deal with the following optimization problem

$$\begin{aligned} \min_{[O_i,\Delta_i]_{i\in\mathcal{M}}} \sum_{l=t}^{t+N_\mathrm{p}-1} \textstyle\sum_{i\in\mathcal{M}} \quad & \big(\alpha C_{o,i} s_i(l+1) \\ & + \beta c_i \delta_i(l) o_i(l) + \gamma \delta_i(l)\big), \end{aligned} \tag{9}$$

where α, β and γ weight respectively the stage inventory costs, the acquisition of new drugs to replenish the stock levels and the effort of the pharmacy service derived from the order placement and deliveries. Here, N_p represents the prediction horizon for the planning, $C_{o,i}$ can be interpreted as a cost of opportunity or inventory cost, c_i represents the average cost of drug i, $O_i = [o_i(t), o_i(t+1), \ldots, o_i(t+N_\mathrm{p}-1)]$ is the sequence of orders for drug i for the current and the next $N_\mathrm{p}-1$ days, and $\Delta_i = [\delta_i(t), \delta_i(t+1), \ldots, \delta_i(t+N_\mathrm{p}-1)]$ is defined analogously for the order placement binary variable. The optimization problem (9) has to be solved every day t subject to the model equations (1) to (3), and the constraints (4) to (8). The first component of the optimal sequence O_i represent the units of drug i to be ordered on day t, while the rest of the sequence is discarded. This planning has to be repeated every day t in a receding horizon fashion.

As can be seen, the optimization problem *merges* different objectives into a single performance index so as to obtain a trade-off between the goals considered. The problem presents several challenging issues, e.g., the bilinear term $\delta_i(t)o_i(t)$, the binary nature of $\delta_i(t)$, the uncertainty derived from the stochasticity of the demand, binding constraints (equations (2), (6), and (8)), and also the size of the problem, for hospitals may work with more than one thousand different drugs. A general strategy to solve this type of problem might be based in the use of branch-and-bound methods, but it is not surprising that simplifications are performed and heuristics are used to simplify the management problem. For example, one could separate the problem in item's sub-problems, solve them in a decentralized fashion, and check afterwards if binding constraints are violated. In any case, the role of the pharmacist is essential to check and guarantee the feasibility of the implemented solution.

III. Data-based Decision Support System

In this section, we describe a data-based model predictive decision support system (hereafter, DB-MPDSS) that we have implemented in a real hospital. In particular, this DB-MPDSS exploits historical records of the drugs and provides useful results to set the size and timing of the orders according to the quantities of units in stock. Also, it learns daily as new data become available in the database. In a broad sense, it can be considered from the viewpoint of human-in-the-loop applications (HIL) within the context of cyber-physical systems, because humans make the final decisions, interact with a real-world process, and provide information to the MPDSS. Figure 4 illustrates the structure of the HIL-MPDSS tested in this paper. Four main interacting components constitute it: the pharmacist, i.e., the person responsible for the pharmacy storage; the meds suppliers; the hospital pharmacy; and the MPDSS, which exploits recorded data to help the human decision-making process.

Hereon, we adopt the following notation: $\mathcal{D}$ is the database containing the historical of demanded and ordered quantities for all $i \in \mathcal{M}$, and $\mathcal{T} = \{1, 2, \ldots, t-1\}$ is the set of days for which there exist data in $\mathcal{D}$, i.e.,

$$\mathcal{D} = \{d_i(\hat{t}), o_i(\hat{t})\}_{\forall i \in \mathcal{M}, \hat{t} \in \mathcal{T}}. \tag{10}$$

Although not explicitly specified, through this paper all probabilities calculations will be based on the data provided by $\mathcal{D}$.

Each day t, the pharmacist provides the DSS with the currently on-hand quantities of each of the meds under study, i.e., $s_i(t)$ for all $i \in \mathcal{M}$, and sets a number of days for which future information is required. Considering the latter, and the information in $\mathcal{D}$, the MPDSS automatically provides the following results:

- Minimum quantity of each med i that should be ordered to obtain 0% probability of stockout during the next n days according to historical data, calculated as
$$o_{i,n}(t) = \max\left(0, \max_{\hat{t}\in\hat{\mathcal{T}}} \sum_{k=\hat{t}}^{\hat{t}+n} d_i(k) - s_i(t)\right), \quad (11)$$
where $\hat{\mathcal{T}} = \{1, 2, \ldots, t-n-1\}$.
- Total cost of the order that ensures a 0% probability of stockout for all meds during the same period, i.e.,
$$C_n(t) = \sum_{i\in\mathcal{M}} c_i o_{i,n}(t). \quad (12)$$
Correspondingly, it could be determined the total amount of items that the pharmacy must order $\sum_i o_{i,n}(t)$.
- Probability of stockout for each med $i \in \mathcal{M}$, assuming that no order is placed, for a different number n of days ahead, i.e.,
$$p_{i,n}(t) = p\left(s_i(t+n) \leq 0\right). \quad (13)$$
where $p(s_i(t+n) \leq 0)$ denotes the probability of $s_i(t+n)$
R2.5. being lower or equal to 0. Notice that $p_{i,n}(t) = 0$ entails that there is no period of length n stored in $\mathcal{D}$ in which the cumulative demand of i surpassed the amount of units in stock. Additionally, note that the stock and demand are related through (3). Thus, it is possible to consider the stochasticity from the viewpoint of the stock.
- Probability of not having stockout for all meds, assuming that no order is placed, i.e.,
$$P_n(t) = \prod_{i\in\mathcal{M}} \left(1 - p_{i,n}(t)\right). \quad (14)$$

That is, on the one hand, the DSS provides the quantities of the minimum drugs that should arrive at the pharmacy to cover the patients' demands according to historical records, and, on the other hand, it assesses the risk of this not occurring. The analysis of data allows a more accurate calculation of these values, which conventionally are estimated based on the pharmacist's experience and intuition. In view of the information contained in Table I and the constraints described in Section II, it is the pharmacist who decides when and how many units of each drug should be ordered to the laboratories. Hence, the MPDSS does not undermine the human decision-making power, but augments the information available for managing the inventory, thus facilitating current and future decisions.

Finally, it must be remarked that the use of the proposed DB-MPDSS policy also involves some risks. To begin with, it is assumed that future demand realizations are contained in the database, which may bias suggested orders due to issues such as extreme demand peaks in the past, abrupt demand increments, and seasonal behaviour, to name a few potential problems. Another simplification is the probability of constraint satisfaction provided in Table I, which is calculated empirically using the available data. To have robust statistical guarantees such as those given in [31], a very large number of scenarios are required and the database may not contain enough data. Even when there are some possibilities to mitigate these issues, e.g., filtering data to remove outliers, generate additional scenarios using resampling methods, etc., their impact must be evaluated.

TABLE I
RESULTS PROVIDED DAILY TO THE PHARMACY SERVICE BY THE DECISION-SUPPORT SYSTEM.

		Numbers of days (n)			
		1	2	$\cdots$	N
Meds (i)	1	$o_{1,1}$	$o_{1,2}$	$\cdots$	$o_{1,N}$
	2	$o_{2,1}$	$o_{2,2}$	$\cdots$	$o_{2,N}$
	$\vdots$	$\vdots$	$\vdots$		$\vdots$
	M	$o_{M,1}$	$o_{M,2}$	$\cdots$	$o_{M,N}$
C_n		$\sum_i c_i o_{i,1}$	$\sum_i c_i o_{i,2}$	$\cdots$	$\sum_i c_i o_{i,N}$
Meds (i)	1	$p_{1,1}$	$p_{1,2}$	$\cdots$	$p_{1,N}$
	2	$p_{2,1}$	$p_{2,2}$	$\cdots$	$p_{2,N}$
	$\vdots$	$\vdots$	$\vdots$		$\vdots$
	M	$p_{M,1}$	$p_{M,2}$	$\cdots$	$p_{M,N}$
P_n		$\prod_i(1-p_{i,1})$	$\prod_i(1-p_{i,2})$	$\cdots$	$\prod_i(1-p_{i,N})$

IV. CASE STUDY AND RESULTS

The proposed DB-MPDSS has been tested during a four-month period in the hospital San Juan de Dios, which is located in the Spanish city of Córdoba. To this end, a group of 11 drugs was selected for the study; all of them supplied by the same laboratory. The hospital pharmacy provided the historical data of demand and orders for these 11 drugs during the last previous two years, which allowed us to calculate the historical evolution of the stock levels. For confidentiality reasons, the name, prices, and further specific information about the drugs are not disclosed in this paper.

During the test period, the stock levels of the 11 drugs under study were introduced daily into the system by the pharmacy service. Considering this, the DB-MPDSS automatically calculated the values described in Section III for periods of 2 to 8 days, that is: minimum order quantities to prevent stockouts during the corresponding number of days (see Table II) and probabilities of this occurring in case no order is placed (see Table III). In the same way, the DB-MPDSS provided the total costs of the orders to assure 0% probability of stockout (also in Table II), which, for the reasons mentioned above, are calculated considering unitary prices $c_i = 1$ for all drugs $i = 1, ..., 11$. It can be seen that the number of items to order increases with the number of days without placing any order due to the progressive increase in the cumulative patients'

TABLE II
ADDITIONAL UNITS OF EACH DRUG NEEDED TO AVOID STOCKOUT FOR 2 TO 8 DAYS, AND TOTAL COST WITH $c_i = 1$, FOR ALL $i = 1, ..., 11$.

		Numbers of days (n)						
		2	3	4	5	6	7	8
Meds (i)	1	0	50	50	50	100	100	150
	2	0	4	8	8	12	16	16
	3	0	0	0	0	0	0	4
	4	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0
	6	0	10	160	240	250	270	350
	7	0	0	0	0	0	0	40
	8	0	0	0	0	20	20	120
	9	0	0	0	0	0	0	0
	10	0	0	0	0	0	0	0
	11	0	0	0	0	0	0	0
C_n		0	64	218	298	382	406	680

TABLE III
INDIVIDUAL AND JOINT PROBABILITY OF STOCKOUT IN 2 TO 8 DAYS WITHOUT ORDERS.

		Numbers of days (n)						
		2	3	4	5	6	7	8
Meds (i)	1	0	0.09	0.28	1.31	2.34	4.40	9.75
	2	0	0.09	0.65	1.59	4.12	7.77	12.93
	3	0	0	0	0	0	0	0.09
	4	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0
	6	0	0.09	0.47	0.84	1.31	2.53	7.59
	7	0	0	0	0	0	0	0.09
	8	0	0	0	0	0.09	0.28	0.75
	9	0	0	0	0	0	0	0
	10	0	0	0	0	0	0	0
	11	0	0	0	0	0	0	0
P_n		1	99,73	98,61	96,31	92,33	85,70	71,94

demands. Accordingly, the joint probability of preventing any stockout decreases with the number of days. In particular, the values given in Tables II and III correspond to a day of the test period in which the stock levels of the drugs where respectively $80, 10, 24, 12, 33, 495, 119, 114, 80, 59$ and 52 units. The reason for setting the minimum period to 2 days is the laboratory transport delay, i.e., all drugs ordered on the day t arrive on the day $t + 2$ in the worst case.

Such tabular data were calculated by the DB-MPDSS and provided to the pharmacy staff, who made the final decisions taking into account all the constraints of the problem (maximum storable stock, minimum order at provider, etc.). During the experiment, the pharmacy service decided when to order depending on the stockout probability they were willing to assume, but the recommendations of the DSS about the quantities were followed faithfully. That is, if the pharmacy placed an order of drug i, then the ordered quantity was that recommended by the DSS to avoid stockout during the number of days considered by the pharmacy manager. Following these recommendations, it has been seen that it is possible to reduce both the number of drugs stored and the number of orders without jeopardizing the satisfaction of the demand.

A. Performance Assessment

To assess the performance of the proposed method during the entire test period, we compare the results with the model predictive control approach proposed in [34], which was previously implemented and tested in this hospital for the same drugs. In particular, figures 5 and 6 show the evolution of the stock levels and the orders placed for the test period during which the data-based decision support system was applied, and the simulation results with the model predictive control (MPC) technique described in [34].

In the simulations shown here, the MPC controller, based on the daily stock data and taking into account the mean demand of the same database, optimizes the number of items to be ordered by minimizing the objective function (9) with $\alpha = \beta = 1$ and $\gamma = 0$ subject to the constraint set (4)-(8). In particular, we have used $N_p = 20$ for the horizon. Also, we have considered a control horizon $N_c = 2$, i.e., the MPC controller decides whether drugs should be ordered the current or the following day. The rest of alternatives are not considered for simplicity. Note that this decision does not affect the performance of the controller when new items are to be ordered in the current day.

For the sake of comparison, we assume that the pharmacy service would follow faithfully the size and timing of the orders recommended by the controller. For a more detailed comparison between the MPC simulation results and the performance of the DB-MPDSS proposed in this paper, Table IV shows the following key performance indicators (KPI) for each of the meds i:

- Mean value (μ_i) and standard deviation (σ_i) of the items in stock.
- Maximum (M_i) and minimum (m_i) registered number of items in stock.
- Number of stockouts (SO_i) registered in the period of study.
- Order rate (OR_i), i.e., the number of days an order for drug i was placed divided by the total number of days in the test period.
- Average size of the orders (AO_i).

Our results show that the MPC controller would have outperformed the DB-MPDSS results in some KPI. As shown in Table V, the average stock of the drugs was reduced with the MPC, saving 649.5 euros, and the number of orders was also

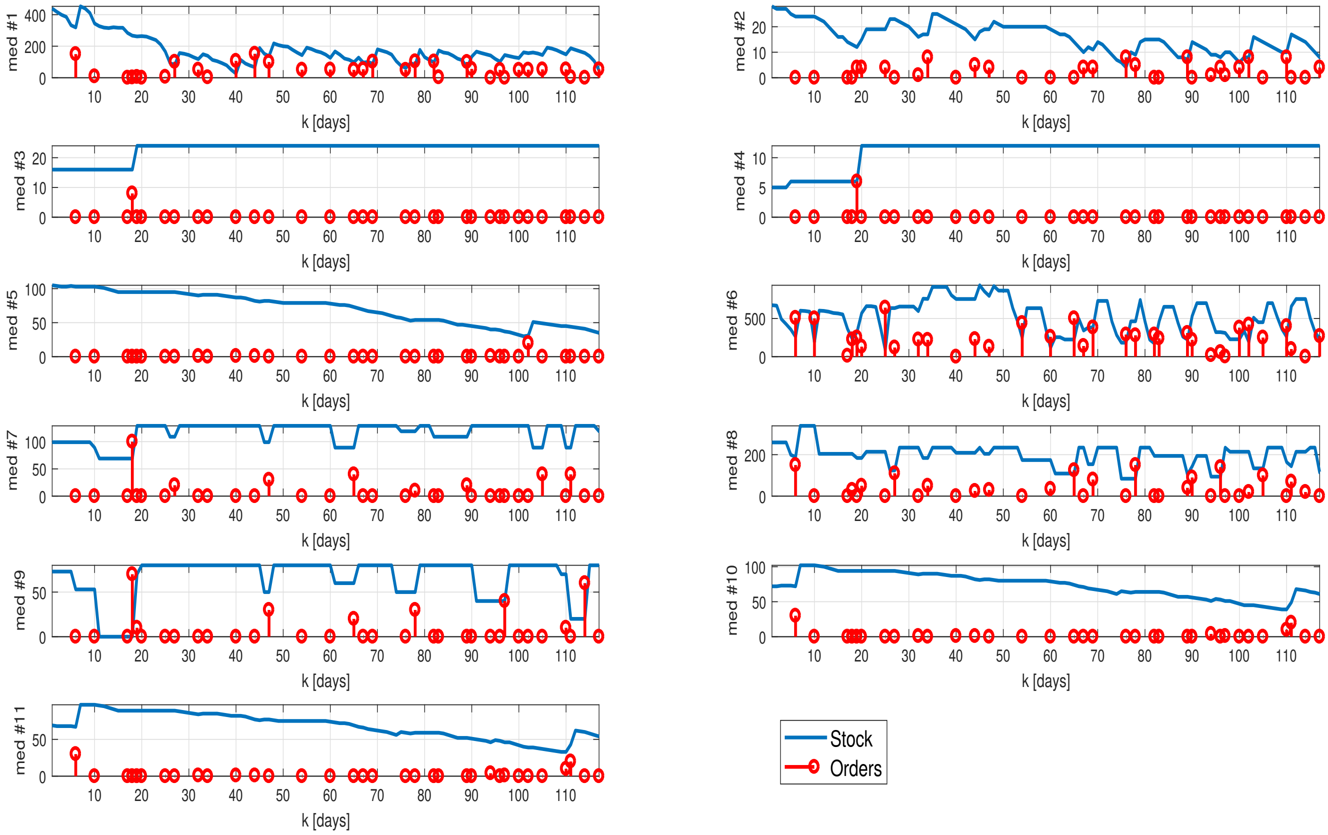

Fig. 5. Evolution of stocks and orders during the test period.

reduced, being 31 days with this technique, compared to 34 with the DB-DSS[2]. However, the improvement comes at a cost in the satisfaction of clinical demands: the MPC method ended up with four stockouts, caused by the differences between the real patients' demands and the average considered for the predictions, hence compromising the patients' safety.

Additionally, in the period before this experiment, the pharmacy was controlling these drugs without the aid of the MPC controller. In Table VI, we show the KPIs obtained during the four months previous to the experiment for the sake of comparison. It can be seen that the overall average of stored items was reduced during the test period of the DB-DSS, and yet the number of stockouts was 0. Also, the maximums reached by the stock levels of each med were reduced or maintained around a similar value. Regarding the number of orders, it decreased from 42 to 34 when implementing the DB-DSS, i.e., a reduction of 19%. However, the average money immobilized in the pharmacy increased in 366.73 € due to a slight increase of the mean stock levels of some of the most expensive drugs, possibly derived from some peaks in the historical demand and the imposed risk stockout events, which was 0%. In this regard, the extra expenditures aim to minimize the risks of stockouts, and indeed, the quantities stored are determined to satisfy past real demands. Accordingly, the lowest values of the most expensive drugs were observed when using the MPC policy as might be expected from (9). Hence, the implementation of the DB-DSS improved the management in most of the KPI with respect to the usual methodology, guaranteeing the satisfaction of the demand, and also providing important advantages such as the reduction of the storage space required and the workload by reducing the number of orders.

Finally, in order to assess the upper bound on performance of MPC-based strategies, it is considered the ideal case of a MPC controller with perfect demand forecast and prediction horizon $N_\mathrm{p} = 5$, which leads to the same number of orders as in the experiment, i.e., 34. In this way, it is possible to focus on the comparison of the management of stock levels. The simulation of this strategy leads to no stockouts with pharmacy savings of 1346.5€. Hence, the performed test with the DB-MPDSS obtained savings that are slightly below the half of those of the theoretical optimum. While this optimal result is not achievable due to the unrealistic assumption of perfect forecast, it suggests that there may be room for further performance enhancements with the proposed method.

[2]The economic savings given were calculated considering the mean stocks and the original unitary prices of the drugs

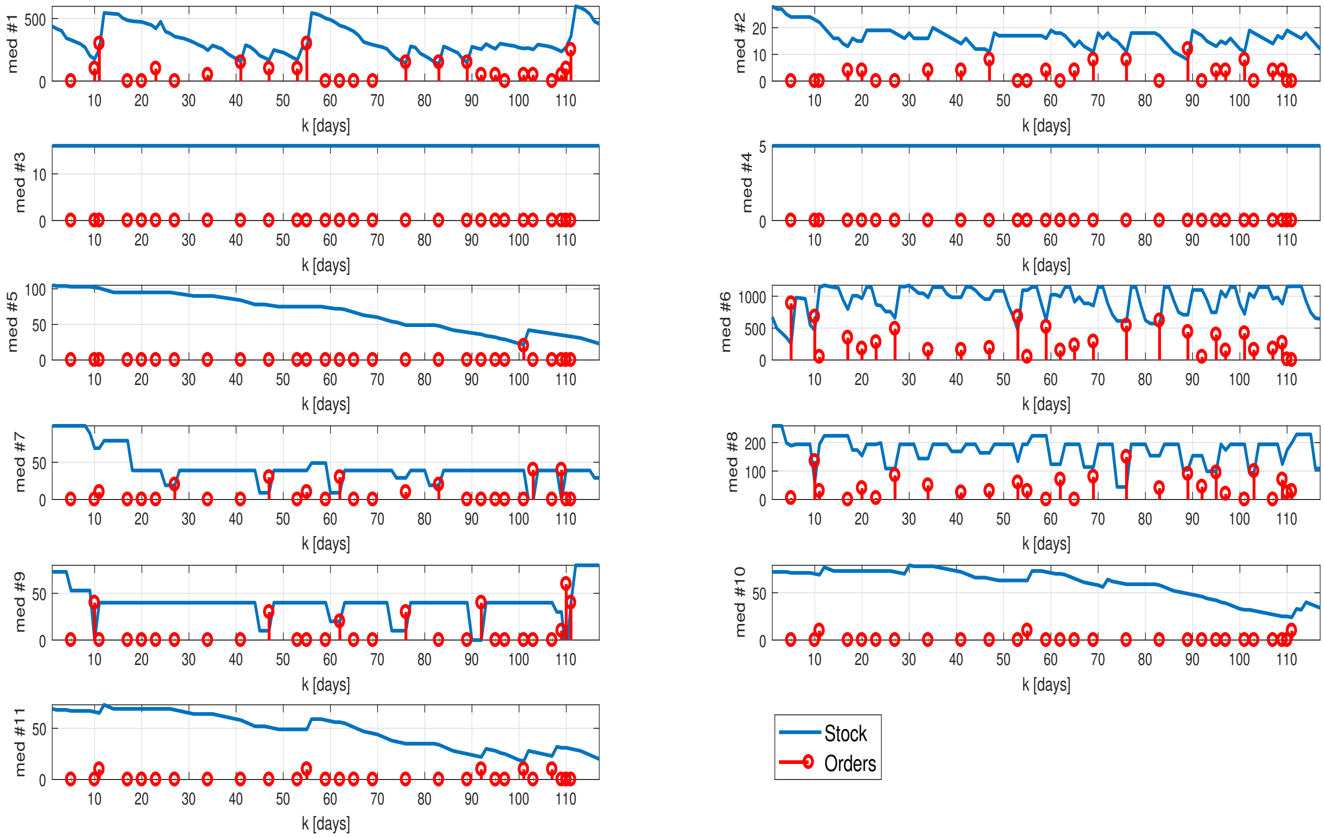

Fig. 6. Evolution of stocks and orders in the MPC simulation [34].

V. Conclusions

In this work, a data-based model predictive decision support system was developed and applied to improve the stock management policy in the pharmacy of the hospital *San Juan de Dios*, located in Córdoba, Spain.

From the viewpoint of the pharmacy staff, the new tool developed increases their security and confidence when placing orders, making them more aware of the risks assumed.In this regard, the risk and orders tables provided by the DB-MPDSS are much richer than information given by the current information system used at the hospital, allowing pharmacists to take better decisions. Likewise, the proposed method reinforces the role of the pharmacist in the inventory management loop and its implementation is simple, i.e., it does not alter the workflows in the pharmacy department, which are relevant aspects to facilitate its adoption.

Also, this contribution has shown improvement with respect to other methods applied, namely, a simple MPC controller and the usual policy of the pharmacy service. In particular, the stock levels have been lowered, and the number of orders has also been reduced. It must be noticed that our test was performed with a small subset of economically inexpensive drugs. Considering that the hospital manages more than 1300 different drugs and that the unit cost of some of them is beyond one thousand euros, any performance improvement that maintains the quality of service level results in significant savings. Moreover, our assessment with respect to a perfect forecast MPC also indicates that there may be room for improving performance, e.g., by filtering extreme past demand peaks from the data.

Therefore, it can be considered that the application of data-based policies in this context is easy to implement and promising due to its positive impact in the pharmacy department, reducing both stock levels and staff workload. This method was considered as a high-value support system by the pharmacy service. This aid is essential in a context where stock management is surrounded by a high degree of uncertainty. For this reason, it is expected to expand the number of drugs controlled in this way by incorporating other providers into the software. In addition, for safety, the software developed was independent of the hospital information system, thus requiring the pharmacy staff to enter the stock data each day manually. This task is tedious and, therefore, another expected improvement is to establish a direct connection with the hospital database. In this way, it will be easier to use the DB-MPDSS in a generalized manner with the rest of the drugs and suppliers.

TABLE IV
KPI COMPARISON BETWEEN THE DB-DSS IMPLEMENTED IN THE EXPERIMENT AND THE OBTAINED SIMULATION RESULTS WITH THE MPC CONTROLLER IN [34].

		μ_i		σ_i		M_i		m_i		SO_i		OR_i		AO_i	
		DB	MPC	DB	MPC	DB	MPC	DB	MPC	DB	MPC	DB	MPC	DB	MPC
Meds (i)	1	174.29	320.13	91.37	117.87	453	598	26	137	0	0	0.250	0.154	59.48	125.00
	2	16.07	16.68	5.56	3.61	28	28	4	8	0	0	0.162	0.154	4.68	5.33
	3	22.78	16.00	2.88	0	24	16	16	16	0	0	0.009	0	8.00	0
	4	11.00	5.00	2.30	0	12	5	5	5	0	0	0.009	0	6.00	0
	5	71.09	66.97	22.94	25.85	105	105	30	22	0	0	0.043	0.009	4.80	20.00
	6	531.17	934.35	218.33	218.10	935	1172	86	253	0	0	0.274	0.256	264.25	288.33
	7	116.20	42.42	18.85	21.74	129	99	69	-1	0	3	0.068	0.077	37.50	23.33
	8	198.32	174.47	53.02	44.96	339	259	84	44	0	0	0.154	0.197	73.06	56.96
	9	65.85	39.37	23.70	16.73	80	80	0	-20	0	1	0.068	0.068	33.75	33.75
	10	73.37	59.69	17.25	15.73	102	79	39	24	0	0	0.068	0.051	8.50	10.00
	11	68.23	47.75	17.46	17.21	97	73	33	18	0	0	0.068	0.043	8.50	10.00

TABLE V
OVERALL PERFORMANCE COMPARISON OF THE DB-DSS AND THE MPC APPROACH IN [34]

	#Orders	Savings [€]	#Stockouts
DB (Experimental results)	34	-	0
MPC (Simulation results)	31	649.5	4

TABLE VI
KPI DURING THE FOUR-MONTHS PERIOD PREVIOUS TO THE EXPERIMENT.

		μ_i	σ_i	M_i	m_i	SO_i	OR_i	AO_i
Meds (i)	1	375.75	87.90	568	183	0	0.265	56.03
	2	13.73	6.43	33	0	0	0.179	10.86
	3	11.94	5.14	21	0	0	0.094	7.27
	4	8.84	1.67	11	6	0	0	0
	5	79.81	31.10	138	3	0	0.137	22.19
	6	828.31	220.95	1355	212	0	0.248	236.45
	7	77.09	23.61	109	9	0	0.068	44.13
	8	292.08	94.35	504	124	0	0.077	144.67
	9	107.03	26.15	173	33	0	0.034	45.50
	10	71.53	17.27	102	40	0	0.171	13.50
	11	75.76	20.07	111	34	0	0.171	13.35

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ARTÍCULOS DE CONGRESO

Capítulo 4

IMPACTO ECONÓMICO DE LA APLICACIÓN DE TÉCNICAS DE CONTROL PREDICTIVO BASADO EN MODELO A LA GESTIÓN DE UN SERVICIO DE FARMACIA

A continuación se presenta una copia de la comunicación aceptada por la Sociedad Andaluza de Farmacia Hospitalaria en su congreso anual de 2010:

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TÍTULO

IMPACTO ECONÓMICO DE LA APLICACIÓN DE TÉCNICAS DE CONTROL PREDICTIVO BASADO EN MODELO A LA GESTIÓN DE UN SERVICIO DE FARMACIA

OBJETIVOS

La gestión del stock presenta problemas fácilmente modelables en el marco de las técnicas de control predictivo basado en modelo (MPC): incertidumbres en la demanda o las cantidades almacenadas, retrasos en la entrega de pedidos, límites máximos y mínimos de unidades, rotación de stock para evitar caducidades, etc. El objetivo de este estudio es demostrar las ventajas resultantes de la aplicación de esta metodología a la gestión de un Servicio de Farmacia de un Hospital de Tercer Nivel.

MÉTODOS

A partir de datos reales de entradas y salidas, se obtiene un modelo que caracteriza el comportamiento de la demanda diaria del medicamento en cuestión, se fijan una serie de datos (cantidad mínima y máxima en stock, mínimo número de unidades por pedido), y se realizan simulaciones con una política de gestión de stock a partir de MPC. Se aplicó esta metodología a 2 medicamentos.

RESULTADOS

En el periodo en estudio se solicitaron 10200 unidades del primer medicamento, distribuidas en 4 pedidos. Se obtuvo una media de 2700 unidades con una desviación típica de 868. Las simulaciones efectuadas arrojan que se podrían haber pedido 8000 unidades repartidas en 4 pedidos, obteniendo una media de 2430 unidades con una desviación típica de 543. De la misma forma se estudió el segundo medicamento, del cual se realizaron 3 pedidos de 80 unidades (240 unidades en total), obteniéndose así un nivel medio de 106 unidades con una desviación típica de 30. Aplicando la misma metodología de simulación, se extrae que se podrían haber pedido 200 unidades en 4 pedidos, obteniendo una media de 59 unidades con una desviación típica de 14. La política implementada por el MPC habría supuesto un ahorro de más de 9000 euros en el periodo considerado (5764 y 3350 euros respectivamente, por las 2200 y 40 unidades de menos solicitadas de cada uno de los medicamentos).

CONCLUSIONES

La simulación efectuada es contundente al comparar ambas políticas de gestión. Al ahorro económico se suman ventajas como la reducción del espacio de almacenamiento y el consiguiente control de caducidades. Se podría disponer de un stock mucho más controlado y estable, gracias al MPC

Capítulo 5

APLICACIÓN DE TÉCNICAS DE CONTROL PREDICTIVO A LA GESTIÓN DE STOCKS EN FARMACIA HOSPITALARIA

A continuación se presenta una copia de la comunicación aceptada por la Sociedad Española de Farmacia Hospitalaria en su congreso anual de 2015:

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TÍTULO

APLICACIÓN DE TÉCNICAS DE CONTROL PREDICTIVO A LA GESTIÓN DE STOCKS EN FARMACIA HOSPITALARIA

OBJETIVOS

La adquisición y almacenamiento de medicamentos son dos de las principales tareas de gestión que lleva a cabo el Servicio de Farmacia de un hospital. Por una parte deben satisfacerse las necesidades clínicas en todo momento, pero las limitaciones económicas y las restricciones logísticas obligan a usar estrategias de compra que permitan almacenar la mínima cantidad. De ahí la importancia de aplicar una buena política de gestión que satisfaga objetivos contrapuestos. El objetivo de esta comunicación es evaluar y comparar tres técnicas de gestión diferentes para optimizar el número de pedidos que realiza el Servicio de Farmacia de un hospital.

MATERIAL Y MÉTODOS

Las técnicas evaluadas se basan en la utilización de un modelo matemático para predecir la evolución del stock a partir de las estimaciones disponibles acerca del comportamiento esperado de la demanda. Este tipo de técnicas son conocidas como Control Predictivo Basado en Modelo. Las técnicas evaluadas son:

1. Gestión con restricciones probabilísticas (GRP), donde se consideran la media y la desviación estándar de los datos históricos de la demanda para garantizar la satisfacción de las restricciones impuestas por el Servicio de Farmacia (por ejemplo, existencias superiores al stock de seguridad) con una cierta probabilidad.

2. Gestión basada en múltiples escenarios (GME), en la que las decisiones de adquisición de medicamentos se toman de forma que se garantice la satisfacción de las restricciones del Servicio de Farmacia en escenarios de evolución de la demanda basados en datos históricos. Es decir, si la demanda sigue

patrones de comportamiento similares a los ya registrados, las restricciones son satisfechas.

3. Gestión basada en árboles de evolución (GAE), que es una variación del método anterior que agrupa los escenarios más probables en un árbol de posibilidades que se va ramificando a la vez que el comportamiento de los escenarios de evolución de la demanda diverge significativamente.

Estas tres técnicas han sido evaluadas en simulación para la gestión de un medicamento termolábil de alto impacto económico.

RESULTADOS

Las metodologías propuestas optimizan la gestión, garantizando el abastecimiento de la demanda, y proporcionando además importantes ventajas como la disminución del espacio de almacenamiento necesario, reducción de la carga de trabajo mediante la reducción del número de pedidos, además de ahorros económicos en base a la disminución del nivel medio de stock. La diferencia entre el caso real y la simulación es lo suficientemente grande, tanto en el número de pedidos realizados como en el promedio almacenado, para considerar que la aplicación de este tipo de políticas en este contexto es prometedora.

Capítulo 6

INNOVACIÓN PARA OPTIMIZACIÓN DE GESTIÓN

A continuación se presenta una copia de la comunicación aceptada por la Sociedad Española de Farmacia Hospitalaria en su congreso anual de 2018:

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TÍTULO

INNOVACIÓN PARA OPTIMIZACIÓN DE GESTIÓN DE STOCKS

OBJETIVOS

La adquisición y almacenamiento de medicamentos es una de las principales tareas de gestión que realiza un Servicio de Farmacia Hospitalaria. Por una parte deben satisfacerse las necesidades clínicas, pero las limitaciones de recursos económicos y las restricciones logísticas obligan a utilizar estrategias de adquisición que minimicen la cantidad almacenada, asegurando, con cierto grado de certeza, que se podrá responder a la demanda en la clínica. De ahí la importancia de aplicar una buena política de gestión que satisfaga dichos objetivos contrapuestos. El objetivo de este estudio es la implantación de nuevos sistemas que mejoren la eficiencia de la gestión en los Servicios de Farmacia Hospitalaria.

MATERIAL Y MÉTODOS

Se ha diseñado un controlador para la optimización del stock mediante técnicas de control predictivo. Para ello se ha seleccionado un proveedor en concreto y 10 medicamentos que se solicitan al mismo. Se han establecido una serie de parámetros como son stock mínimo, stock máximo almacenable, embalaje, pedido mínimo al proveedor, tiempo estimado de entrega de pedidos, etc. y, teniendo en cuenta también los consumos de los 12 meses anteriores, se ha diseñado un algoritmo que automatiza la gestión de inventario explotando las sinergias existentes entre los pedidos a un mismo proveedor. Para ello, el controlador simula la evolución esperada de los niveles de stock durante un intervalo de tiempo, calculando así el pedido óptimo para el conjunto de medicamentos considerado.

Durante un periodo de 4 meses se han introducido diariamente en el programa desarrollado los datos de stock de los 10 medicamentos en cuestión y de forma automática el software ha calculado el pedido para dicho grupo de medicamentos. Desde el Servicio de Farmacia se ha seguido fielmente la recomendación del controlador a la hora de realizar los pedidos.

RESULTADOS Y CONCLUSIONES

Durante estos 4 meses, en comparación con el mismo periodo del año anterior, se han reducido considerablemente tanto el número de pedidos al proveedor como el stock promedio de estos medicamentos. Se ha estimado un ahorro económico de 644.89 euros y además se ha reducido la carga de trabajo en el Servicio de Farmacia. No se ha producido ninguna rotura de stock.

La metodología propuesta ha mejorado la gestión a diferentes niveles: garantiza el abastecimiento con una disminución del nivel de inventario y del número de pedidos, lo que libera espacio y reduce la carga de trabajo, además de generar ahorros económicos.

Se puede considerar que la aplicación de este tipo de políticas en este contexto es prometedora además de fácil de implementar. Como línea futura de trabajo se pretende ampliar la cantidad de medicamentos controlados de esta forma automatizada mediante la incorporación de otros proveedores al programa, con la intención de validar también otra de las técnicas que han sido propuestas durante el periodo de investigación en este campo y que hasta el momento sólo han podido ser estudiadas a nivel de simulación.

PALABRAS CLAVE Gestión Optimización Pedido

Capítulo 7

GESTIÓN y RIESGO DE ROTURA DE STOCK

A continuación se presenta una copia de la comunicación aceptada por la Sociedad Española de Farmacia Hospitalaria en su congreso anual de 2019:

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TÍTULO

GESTIÓN y RIESGO DE ROTURA DE STOCK

OBJETIVOS

Un Servicio de Farmacia debe disponer de niveles de stock suficientes para atender las necesidades clínicas del hospital (pacientes ingresados, consultas, quirófanos, hospital de día, pacientes externos, etc...) pero el elevado impacto económico de muchos medicamentos y las restricciones presupuestarias obligan a optimizar la gestión, evitando el dispendio de recursos y la aparición de problemas relacionados con la falta de espacio o las caducidades. Además, debe tenerse en cuenta también el impacto que la política de pedidos tiene sobre la carga de trabajo del personal en el Servicio de Farmacia.

El objetivo de este trabajo es la mejora de la eficiencia de la gestión en los Servicios de Farmacia Hospitalaria mediante un software que estima de riesgo de rotura de stock, haciendo diferentes propuestas de pedidos y sirviendo como herramienta de soporte a la toma de decisión del personal de farmacia.

DISEÑO

Se ha seleccionado un proveedor y 11 medicamentos que se solicitan al mismo junto con parámetros como stock mínimo y máximo, embalaje, pedido mínimo y tiempo estimado de entrega de pedidos. Asimismo, se proporcionan al programa los consumos de los 24 meses anteriores. El software calcula, partiendo del nivel de inventario actual, la probabilidad de rotura de stock de cada medicamento durante los 8 días siguientes utilizando para ello los históricos de demanda suministrados. Además, propone al farmacéutico las cantidades necesarias para garantizar el abastecimiento para cada uno de los días, indicando el coste y el impacto en términos de probabilidad de rotura.

CIRCUITO Y ETAPAS

Recopilación de datos a parametrizar, históricos de consumos, diseño y validación real.

IMPLANTACIÓN

Durante un periodo de 3 meses se ha utilizado el programa como herramienta de ayuda a la toma de decisión en el Servicio de Farmacia, valorando sus propuestas para 2, 3, 4 ó 5 días, el importe del pedido en cada caso, y la probabilidad de rotura de stock si no se hiciese pedido.

RESULTADOS Y LIMITACIONES

Durante estos 3 meses, en comparación con el mismo periodo del año anterior, se han reducido considerablemente tanto el número de pedidos al proveedor (un 30 % menos) como el stock promedio de estos medicamentos (579 unidades menos). No se ha producido ninguna rotura de stock.

El diseño actual requiere introducir manualmente los datos de stock, lo que dificulta la extensión a más medicamentos. Como mejora, se considerará la conexión directa del sistema con el programa de gestión del centro para tomar los datos directamente.

APLICABILIDAD A OTROS SERVICIOS DE FARMACIA

La metodología propuesta para optimizar el stock ha demostrado mejorar la gestión, garantizando el abastecimiento de la demanda en todo momento, y proporcionando además importantes ventajas como la disminución del espacio de almacenamiento necesario, reducción de la carga de trabajo mediante la reducción del número de pedidos, además de ahorros económicos en base a la disminución del nivel medio de stock.

La gran ventaja del programa es la confianza que proporciona al personal respecto al abastecimiento de la demanda con unos niveles de incertidumbres controlados. Por ello, este método es un soporte de gran valor y una herramienta aplicable para mejorar la gestión de un Servicio de Farmacia.

PALABRAS CLAVE Gestión Riesgo Stock

ARTÍCULOS DE REVISTA

Capítulo 8

GESTIÓN DE INVENTARIOS EN HOSPITALES USANDO CONTROL PREDICTIVO CON RESTRICCIONES DE PROBABILIDAD

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Stock management in hospital pharmacy using chance-constrained model predictive control ☆

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Pharmacy Management Stockout Risk

ABSTRACT

One of the most important problems in the pharmacy department of a hospital is stock management. The clinical need for drugs must be satisfied with limited work labor while minimizing the use of economic resources. The complexity of the problem resides in the random nature of the drug demand and the multiple constraints that must be taken into account in every decision. In this article, chance-constrained model predictive control is proposed to deal with this problem. The flexibility of model predictive control allows taking into account explicitly the different objectives and constraints involved in the problem while the use of chance constraints provides a trade-off between conservativeness and efficiency. The solution proposed is assessed to study its implementation in two Spanish hospitals.

1. Introduction

Stock management is a common problem that is present in almost all the companies and organizations. The solution for this problem is given by a policy that determines how and when the orders should be placed. However, there are different difficulties associated to the problem. In the first place, there are uncertainties in the demand and delays in the deliveries, which make the problem not deterministic and require a degree of conservatism to avoid stockouts. It is needless to say that the lack of certain drugs in a hospital may endanger the life of the inpatients and, in the worst case, may have catastrophic consequences in the form of human losses. In order to avoid this situation, it is preferred to increase stock levels, but this is not always possible due to economical constraints. Actually, the pharmacy is a major source of expenses in hospitals. In [1], it is estimated that about 20–35% of the goods budget of a public hospital is spent by the pharmacy department. In a wider sense, the limitations imposed by the budget are also translated into the human resources in the pharmacy and the room available for storing drugs, which introduce additional constraints for the management. Hence, it may not be possible to place and receive orders too often due to the lack of pharmacists. Likewise, space constraints are important for example in drugs that must be stored in a fridge. Therefore, there is a need to develop advanced cost-efficient safe policies for stock management in hospitals capable of dealing with many different types of constraints.

In general, simple methods are used to solve inventory control problems. A usual policy is that of reorder point (s, S), that is, whenever the stock is below the level s, an order is placed to increase the stock up to the value S. Another option is to fix a size for the orders, Q, and submit an order once the stock is at level s. Other related policies about how to solve this problem are given in [2,3]. The major drawback with these techniques is that they are not able to take into account all the factors involved in the decision problem. In the literature, other alternatives are also proposed. For example, Bermejo et al. [4] presents an analytical model for the coordination of inventory and transportation in supply-chain systems. In [5], a supply chain network model consisting of manufacturers and retailers, where the demand is random, is developed.

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More strategies are presented in [6], where a competitive and cooperative selection of inventory policies in a supply chain with stochastic demand are studied. On the other hand, Rezapour and Farahani [7] develops a model to design a supply chain network with deterministic demand.

In this work, a model predictive control (MPC) strategy is proposed given the flexibility offered by its framework to handle multi-variable interactions, constraints on the problem variables, and optimization requirements in a systematic manner. Moreover, MPC has been successfully applied in the industry [8] and in similar problems. Some works based on the application of MPC are, for example, [9,10], where MPC is used to supply chain management in semiconductor manufacturing. Another example can be found in [11], where a distributed MPC algorithm with low communication burden is tested by using the MIT Beer Game (a supply chain benchmark). An extension of this scheme for systems with more than two controllers is also tested with supply chains in [12]. In [13], a robust MPC technique is used in a production-inventory system. Finally, in [14] the problem of managing inventories and supply chains is treated to reduce the number of tuning parameters with a technique based on a variation of MPC.

In the particular case of the stochastic control problems, i.e., those where the system being controlled is subject to uncertainties and/or unknown disturbances, the control policy can guarantee that the actual variables do not violate the constraints at the cost of an additional conservatism. That is, the actions implemented by the control policy are designed to deal with worst-case scenarios, which results in a waste of resources [15]. In this situation, it is acceptable to assume a low level of risk to save resources. To this end, the original constraints of the problem can be formulated in a probabilistic manner. The use of *chance constraints* was introduced in [16] and has been studied in a stochastic programming framework [17].

The implementation of MPC in combination with chance constraints is known as chance-constrained MPC (CC-MPC). The rationale of this approach is to replace hard constraints with probabilistic constraints and the nominal cost function with its expected value in the MPC formulation [18], leading to a stochastic optimization problem. CC-MPC offers advantages as robustness, flexibility, low computational requirements, and the possibility of including the level of reliability associated with the constraints [19,20]. Furthermore, since CC-MPC takes into account the expected performance of the closed loop with probabilistic constraints instead of directly trying to assure robust constraint satisfaction, it avoids the conservatism present in other robust MPC techniques, e.g.: [21,22].

There are other alternatives in the stochastic MPC literature that are also suitable for this type of problem. One option to deal with constraints on the inputs and states while optimizing some performance criterion, also in the presence of uncertainties or disturbances, is the scenario-based MPC method proposed in [23]. This method is based on the optimization of the control inputs over a finite horizon, subject to robust constraints under a finite number of random scenarios of the uncertainty and/or disturbances. A different but related approach is tree-based MPC [24], where the disturbances are grouped into a rooted tree that branches as the uncertainty grows. A tree of control actions is calculated to match the disturbance tree by the MPC controller. A simpler method is multiple MPC, which is given in [25], where control actions are calculated weighting the probability of occurrence of three possible scenarios. While all these approaches could be valid in for the problem considered in this article, they present some disadvantages with respect to CC-MPC. In the first place, scenario-based MPC requires a great amount of historical data to provide a low risk level. Tree-based MPC also requires a amount of historical data and solves a problem with a larger number of optimization variables, i.e., the computational burden of this method is greater. Finally, multiple MPC oversimplifies the computation of the control actions due to the low number of scenarios considered. In addition, all these methods have in common that the existence of a very severe scenario may result in an increase of conservativeness [26].

In this paper, which is an extension of the previous works [27,28], CC-MPC is used to solve the problem of inventory management in hospital pharmacies. In particular, the formulation of the problem is generalized with respect to the aforementioned works, where a Gaussian behavior of the demand is assumed. The mathematical development of the controller presented here can be applied even if the demand is only characterized statistically based on historical data. Likewise, the case of several hospitals that cooperate in order to relax their risk levels is another contribution of this work. It must be also remarked that this article has been carried out in the context of a project named *Pharmacontrol*, whose goal is to improve the inventory management in two Spanish hospitals.

The remainder of the paper is organized as follows. First, a description of the pharmacy inventory management optimization problem is shown in Section 2. Section 3 presents the MPC statement for this problem. In Section 4, some simulations are shown and the corresponding results are discussed. Finally, in Section 5 the conclusions are drawn.

2. Pharmacy inventory management

In this section, the mathematical background needed to build the optimization problem to be solved by the CC-MPC is presented.

2.1. System definition

In general, it will be assumed that there are N_i different drugs in the pharmacy inventory. The stock level of each one follows an evolution depending on the orders and on the demand. This evolution is represented by a discrete linear model, which for the particular case of drug i is

$$s_i(t+1) = s_i(t) + \sum_{j=1}^{np_i} o_i^j(t-\tau_i^j) - d_i(t), \tag{1}$$

where $s_i \in \mathbb{Z}$ is the stock of drug i, $o_i^j \in \mathbb{Z}$ is the number of ordered items to the j-th of the np_i providers of the drug i, τ_i^j is its corresponding transport delay, and $d_i(t)$ represents the aggregate demand of drug i.

The number of ordered items can be modeled as $o_i^j = \delta_i^j(t-\tau_i^j)o_i^j(t-\tau_i^j)$, where $\delta_i^j(t)$ is a Boolean variable, that is, $\delta_i^j(t) = 1$ if an order of drug i to provider j is placed during time t, otherwise $\delta_i^j(t) = 0$, and $o_i^j \in \mathbb{Z}$ represents the number of ordered items of drug i to provider j, only in those cases where $\delta_i^j(t) = 1$.

2.2. Single hospital optimization problem

The system can be represented according to Fig. 1. In this figure, the inputs represent the elements considered by the pharmacy managers to make the decisions about the order placement: the estimated demand, information about potential risks, and the constraints. The outputs are the optimal stock levels, minimum costs, and data about when and how many orders should be placed.

Every time an order is placed, the following costs are involved:

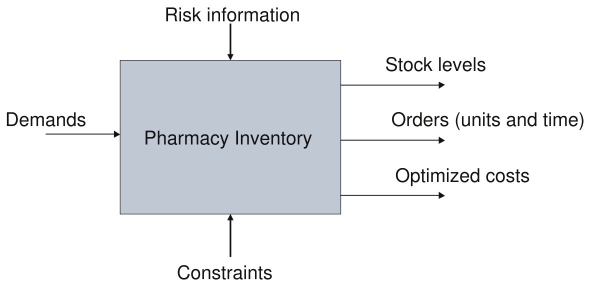

Fig. 1. Pharmacy inventory as a system.

- p_i^j, which is price offered by the j-th provider for drug i. It is supposed in this paper that it does not depend on the number of items ordered.
- $C_{sh,i}^j$, which is the drug i shipping cost when requested from provider j.
- $C_{op,i}$, which is the cost of ordering drug i.
- $C_{os,i}$ is a cost that penalizes when the stock of drug i is below the minimum safety level allowed. This situation is particularly dangerous since there is a high risk for the hospital of running out of drug i. In case of need, it is possible to ask another hospital for a loan.
- $C_{s,i}$ is the cost of storage of drug i.
- $C_{o,i}$ is the opportunity cost of having drug i in the pharmacy storage.

Note that both stock levels and costs are a direct consequence of the orders placed. Finally, the goals of the managers are the following: (i) the demand has to be satisfied; (ii) the fixed assets must be reduced; and (iii) the number of orders placed has to be minimized. These goals are considered in the optimization problem. In particular, the performance index considered in this work involves a multicriteria weighted function where demand satisfaction, expenses and number of orders are included, i.e.,

$$\min_{o} J := \beta_1 J_1(o,t) + \beta_2 J_2(o,t) + \beta_3 J_3(o,t), \tag{2}$$

where J_1, J_2 and J_3 are the terms associated to demand satisfaction, costs, and orders, respectively. The weights β_1, β_2, and β_3 prioritize the different terms and have a strong influence in the solution of the problem.

The terms in the objective function 2 are described next in decreasing priority:

1. J_1: Demand satisfaction. The main objective is the minimization of stockout probability. The main issue here is that the demand is not known in advance, i.e., it is stochastic. There may also be uncertainty in the transport delays. For this reason, it is usual in practice to set a safety stock to mitigate the impact of uncertainty. There are two possibilities in the way the safety stock is set: it can be either fixed or variable. The former proposes that the minimum stock level is introduced as a fixed parameter in the optimization problem. The latter treats the safety stock as an optimization variable. This term is expressed as

$$\min_{\delta_i^j, o_i^j \ \forall i,j} \sum_{k=0}^{N} \sum_{i=1}^{N_i} C_{os,i} \lambda_{\text{stockout}}^i, \tag{3}$$

with

$$\lambda_{\text{stockout}}^i = \begin{cases} 1 & \text{if } s_i(t+k) < S_{\min}^i, \\ 0 & \text{if } s_i(t+k) > S_{\min}^i, \end{cases} \tag{4}$$

where $\lambda_{\text{stockout}}^i$ indicates whether the safety stock condition is violated, $S_{\min}^i$ is the minimum stock level allowed for the drug i, N is the length of the time horizon in which the condition has to be satisfied, and N_i is the number of different drugs.

2. J_2: Expenses. This term deals with the minimization of the expenses in the orders of drugs and the inventory levels, i.e.

$$\min_{\delta_i^j, o_i^j \ \forall i,j} \sum_{k=0}^{N} \sum_{i=1}^{N_i} \sum_{j=1}^{np_i} \delta_i^j(t+k)(p_i^j o_i^j(t+k) + C_{sh,i}^j) + \sum_{k=0}^{N} \sum_{i=1}^{N_i} C_{s,i} s_i(t+k) + \sum_{k=0}^{N} \sum_{i=1}^{N_i} C_{o,i} s_i(t+k). \tag{5}$$

3. J_3: Orders. This term seeks the minimization of the number of placed. It is necessary because placing an order involves a certain cost. Likewise, the work burden for the staff in the pharmacy department is related to this term. For example, in a hospital such as Reina Sofía (Córdoba, Spain) more than twelve thousand orders are placed during a year. Mathematically, it is formulated as

$$\min_{\delta} \sum_{k=0}^{N} \sum_{i=1}^{N_i} \sum_{j=1}^{np_i} C_{op,i} \delta_i^j(t+k). \tag{6}$$

Furthermore, the following constraints are considered:

- *Storage constraints.* As explained before, the level of the stock of drug i has to be greater than a safety stock $S_{\min}^i$ to minimize the risk of stockout. In addition, the space restrictions in the storage room must also be considered, which limits the maximum number of drugs that can be stored in the pharmacy. Therefore,

$$s_i \in [S_{\min}^i, S_{\max}^i]. \tag{7}$$

- **Order constraints.**In order to formulate these constraints, two type of variables are going to be used. The first one is a Boolean variable $\delta_i^j(t) \in [0,1]$, where the value 1 means that an order of drug i has been placed to provider j during time t, and the value 0 means that no order has been placed. In case of placing an order ($\delta_i^j(t) = 1$), another variable that represents the ordered number of items is used. This variable should be bounded by both a minimum and a maximum values, i.e.

$$o_i^j \in [\min_{o_i^j}, \max_{o_i^j}]. \tag{8}$$

There are also some considerations about the minimum number of items to order:

- The distributors do not work if the number of items ordered is too low. Hence, there is a minimum of items to order at each time, $\min_{\text{item}_i^j}$. Likewise, the pharmaceutical laboratories require a minimum amount of money to be spent. That is translated into a minimum order size, $\min_{\text{lab}_i^j}$. Taking into account these quantities

$$\min_{o_i^j} = \max(\min_{\text{item}_i^j}, \min_{\text{lab}_i^j}).$$

- **Non-working days**of the laboratory (e.g., Sundays, holidays) must be taken into account, which leads to the following constraint:

$$\delta_i^j(t) = 0, \quad \forall t \notin \{\text{working days}\}. \tag{9}$$

- **Operational constraints.**These constraints take into account the limited capacity of the pharmacy for placing orders and receiving shipments. This fact limits the number of orders placed along a time horizon of length N, i.e.,

$$\sum_{k=0}^{N}\sum_{j=1}^{np_i}\delta_i^j(t+k)\le\Delta_i, \tag{10}$$

where Δ_i is the maximum number of orders of drug i that can be placed along N.

- **Economical constraints.** The money spent during the time horizon N is also limited, being $\max_\$$ the maximum amount. The constraint is expressed as

$$\sum_{k=0}^{N}\sum_{i=1}^{N_i}\sum_{j=1}^{np_i}\delta_i^j(t+k)(p_i^j o_i^j(t+k)+C_{sh,i}^j+C_{op,i})\le\max_\$). \tag{11}$$

2.3. Cooperation between different hospitals

Different hospitals can cooperate to reduce their safety stocks in case they are close and the consumption of certain drugs is uncorrelated between them. Consequently, the expenses derived from loans between them are low or can even be neglected. This way, the hospitals can focus on the joint stockout probability instead of the individual one, which should be higher, resulting in lower safety and average stock levels. In the simplest case, each hospital would solve its original optimization problem with different constraints. Likewise, it is also possible to formulate this problem in the context of distributed control, where the hospitals are agents that have to reach a consensus on the safety levels. The optimization problem is

$$\min_o \sum_{h=1}^{H} J_h, \tag{12}$$

where J_h stands for the cost of each hospital and H is the number of collaborating hospitals. The overall objective function taking is given by

$$J_h=\sum_{i=1}^{3}\sum_{j=1}^{H}\beta_{i,j}J_{i,j}(o,t),$$

where the demand, expenses, and orders terms are like in (3)–(6). The difference here is that, in the demand term, the probability $Pr(s_i^h(t+k)<0)$ can be greater.

The constraints are also the same, (7)–(11), and

$$s_i^h(t+1)=s_i^h(t)+\sum_{j=1}^{np_i}o_i^{j,h}(t-\tau_i^j)-d_i^h(t), \quad \forall h\in\{1,\dots,H\}. \tag{13}$$

3. Model predictive control

The control strategy used to solve the stock management problem is MPC. This strategy is a control method based on output predictions over a *prediction horizon* (N) calculated using a model of the process [8]. From the optimization of the objective function subject to constraints, a set of future control signals is obtained. Only the control value computed for the time instant k is applied to the process, the rest of them are discarded. This process is repeated in a receding horizon fashion.

3.1. MPC setup

In this section, the implementation of the control problem will be detailed. The objective is the minimization of the objective function (2). Consider the system defined by

$$s(t+1)=s(t)+o(t-\tau)-d(t), \tag{14}$$

where $s(t)=[s_1(t),\dots,s_{N_i}(t)]$, $d(t)=[d_1(t),\dots,d_{N_i}(t)]$ and $o(t-\tau)=\sum_{j=1}^{np_i}\delta_i^j(t-\tau_i^j)u_i^j(t-\tau_i^j)$ represents the total number of items ordered. Note that system (14) is equivalent to (1).

The control variables taken into account in this problem are $\delta_i^j(t)$ and $o_i^j(t)$, both components of the control variable $o(t)$. Solving the optimization problem by using directly the control variable $o(t)$ (i.e., $\delta_i^j(t)$ and $o_i^j(t)$ together) is a difficult task, since they have different nature because $\delta_i^j(t)$ is a Boolean variable. The way to proceed will be the use of an exhaustive search algorithm, which will solve the problem as many times as possible scenarios depending on the value of $\{\delta_i^j(t),\dots,\delta_i^j(t+N)\}$, i.e., $2^{np_i\times N_i(N+1)}$ times. In that way, the optimization problem can be solved with respect to the variable $o_i^j(t)$.

It is straightforward to see that if $\delta_i^j(t+k)=0$, for $k\in\{0,1,\dots,N\}$, the quantity of ordered items is $o_i^j(t+k)=0$. Furthermore, the variable $o_i^j(t)$ can be considered as a real one to relax the problem. Notice that the solution obtained is still integer due to the problem features. In addition, the vector of control variables $\{o_i^j(t),\dots,o_i^j(t+N)\}$ is reduced by eliminating the components $o_i^j(t+k)$ that are equal to zero. Hence,

$$\forall\,\delta_i^j(t+k)=0, \quad k\in\{0,1,\dots,N\},$$

then

$$\underbrace{\begin{bmatrix} o_i^j(t)\\ \vdots\\ o_i^j(t+k)\\ \vdots\\ o_i^j(t+N)\end{bmatrix}}_{\mathbf{o}_i^j(t)} \rightarrow \underbrace{\begin{bmatrix} o_i^j(t)\\ \vdots\\ o_i^j(t+k-1)\\ o_i^j(t+k+1)\\ \vdots\\ o_i^j(t+\tilde{N})\end{bmatrix}}_{\tilde{\mathbf{o}}_i^j(t)},$$

where $\mathbf{o}_i^j(t)\in\mathbb{R}^{N+1}$ and $\tilde{\mathbf{o}}_i^j(t)\in\mathbb{R}^{\tilde{N}+1}$ is a reduced vector of non-zero orders, where

$$\tilde{N}=N-\sum_{k=0}^{N}\left(1-\delta_i^j(t+k)\right),$$

is the number of non-zero orders.

The vector reduction from $\mathbf{o}_i^j(\mathbf{t})$ to $\tilde{\mathbf{o}}_i^j(t)$ can be represented by the following change of variable

$$\mathbf{o}_i^j(t)=M\tilde{\mathbf{o}}_i^j(\mathbf{t}),$$

where $M\in\mathbb{R}^{(N+1)\times(\tilde{N}+1)}$ is a matrix that reduces the dimension of the order vector $\mathbf{o}_i^j(t)$ depending on the value of $\delta_i^j(t)$. It is defined as

$$M(i,j)=\begin{cases}1 & \text{if } \delta_i^j(t)=1\wedge i=j,\\ 0 & \text{if } \delta_i^j(t)=0\vee i\ne j.\end{cases} \tag{15}$$

As direct consequence, $\tilde{\mathbf{o}}_i^j(\mathbf{t})$ contains only non-null components, i.e., the orders that are non-zero.

Taking into account the integer nature of the variable $\delta_i^j(t)$, the resulting optimization problem is a mixed integer one (MIP). There are different techniques to solve them like branch and bound [29], genetic algorithms [30] or the cutting-plane method [31]. In this article, an exhaustive search approach has been implemented. This means that the optimization problem is solved for each possible realization of $\{\delta_i^j(t),\dots,\delta_i^j(t+N)\}$. This way, Boolean variables are removed from the optimization. The optimal solution corresponds with the combination of the values of $\{\delta_i^j(t),\dots,\delta_i^j(t+N)\}$ that provides the minimal value of the objective function.

Remark 1. It is necessary to pay special attention to the constraints while solving this problem. It is not possible to impose the whole matrix of constraints to the reduced vector $\tilde{\mathbf{o}}_{\mathbf{i}}^{\mathbf{j}}(\mathbf{t})$, so it is necessary to apply the change matrix M to the matrix of constraints to impose them only to the considered control components.

3.2. CC-MPC

The CC-MPC method is used to deal with the stock management problem because the constraints under consideration must be treated in stochastic manner. The optimization problem can be written as in (12), but subject to

$$\overline{G}_i(o,\overline{d}) \le g_i,\ i=1,2,\dots,m,$$
$$o \in D,$$

where $D \subset \mathbb{R}^n$, $\overline{d}$ is a stochastic vector defined over a set $E \subset \mathbb{R}^s$, and m is the number of constraints. It is assumed that there is a set of events F, formulated by subsets from E and a probability distribution P, defined over F. Hence, for each $A \subset E$, the probability $P(A)$ is known. In addition, it is assumed that the functions $\overline{G}_i(o,\cdot): E \to \mathbb{R},\ \forall o,\ i$ are random variables and the probability distribution P is independent of the decision variable o.

For addressing this problem, it is necessary to rewrite the optimization problem as a deterministic equivalent in which the constraints are verified with a certain probability. These stochastic constraints are called *chance constraints*. These constraints can be formulated by two different manners as discussed below.

Joint Chance Constraint: The stochastic formulation of the joint chance constraints is given by the objective function (12), subject to

$$P(\overline{G}_i(o,\overline{d}) \le g_i,\ \forall\ i) > 1-\delta_x,$$
$$o \in D,$$

where $\delta_x \in [0,\ 1]$ is the risk that the constraints of the optimization problem are not fulfilled.

Individual Chance Constraint: Individual chance constraints are formulated with the same objective function (12), subject to

$$P(\overline{G}_i(o,\overline{d}) \le g_i) > 1-\delta_{x_i},\ \forall\ i$$
$$o \in D,$$

where it writes one equivalent by each stochastic constraint.

The aggregate demand $d(t)$ in (14) includes a stochastic disturbance component given its uncertain nature. Due to the presence of these uncertainties, the constraints have a stochastic nature, i.e., they can not be written as deterministic ones. Therefore, the constraints can be expressed as

$$P(s(t+k) \ge S_{\min}) \ge 1-\delta_s, \quad \forall k \in \{1,..,N\},$$

where δ_s is the probability of having less stock than $S_{\min}$. This expression can be developed along N and obtain the mean and standard deviation of the state.

For the first time instant along N (i.e., $k=1$), it yields

$$P(s(t+0)+o(t+0)-d(t+0) \ge S_{\min}) \ge 1-\delta_s,$$
$$P(-d(t+0) \ge S_{\min}-s(t+0)-o(t+0)) \ge 1-\delta_s,$$
$$P(\underbrace{d(t+0)}_{Random} \le \underbrace{-S_{\min}+s(t+0)+o(t+0)}_{Deterministic}) \ge 1-\delta_s,$$

which can be rewritten as

$$\phi_0(-S_{\min}+s(t+0)+o(t+0)) \ge 1-\delta_s,$$

where $\phi_0(\cdot)$ is the cumulative distribution function of the random variable $d(t+0)$. The deterministic equivalent for this chance constraint is

$$-S_{\min}+s(t+0)+o(t+0) \ge \phi_0^{-1}(1-\delta_s),$$
$$-o(t+0) \le -S_{\min}+s(t+0)-\phi_0^{-1}(1-\delta_s).$$

For the next time instant along N (i.e., $k=2$), it yields

$$P(s(t+2) \ge S_{\min}) \ge 1-\delta_s$$
$$P(s(t+1)+o(t+1)-d(t+1) \ge S_{\min}) \ge 1-\delta_s$$
$$P((s(t+0)+o(t+0)-d(t+0))+o(t+1)-d(t+1) \ge S_{\min}) \ge 1-\delta_s$$
$$P(-d(t+0)-d(t+1)) \ge S_{\min}-s(t+0)-o(t+0)-o(t+1)) \ge 1-\delta_s,$$
$$P(d(t+0)+d(t+1) \le -S_{\min}+s(t+0)+o(t+0)+o(t+1)) \ge 1-\delta_s.$$

Defining $\phi_1(\cdot)$ as the cumulative distribution function of the variable $d(t+0)+d(t+1)$ yields

$$\phi_1(-S_{\min}+s(t+0)+o(t+0)+o(t+1)) \ge 1-\delta_s,$$
$$-S_{\min}+s(t+0)+o(t+0)+o(t+1) \ge \phi_1^{-1}(1-\delta_s),$$
$$o(t+0)+o(t+1) \ge S_{\min}-s(t+0)+\phi_1^{-1}(1-\delta_s),$$
$$-o(t+0)-o(t+1) \le -S_{\min}+s(t+0)-\phi_1^{-1}(1-\delta_s).$$

Iteratively (e.g., $k=3$) and according to the previous development, it can written as

$$-o(t+0)-o(t+1)-o(t+2) \le -S_{\min}+s(t+0)-\phi_2^{-1}(1-\delta_s),$$

where $\phi_2(\cdot)$ denotes the cumulative distribution function of the variable $d(t+0)+d(t+1)+d(t+2)$.

Generalizing for a prediction horizon N,

$$-\begin{bmatrix} 1 & 0 & 0 & \cdots & 0 \\ 1 & 1 & 0 & \cdots & 0 \\ 1 & 1 & 1 & \cdots & 0 \\ \vdots & & & & \vdots \\ 1 & 1 & & \cdots & 1 \end{bmatrix} \begin{bmatrix} o(t+0) \\ o(t+1) \\ o(t+2) \\ \vdots \\ o(t+N-1) \end{bmatrix} \le \begin{bmatrix} 1 & 1 \\ 1 & 1 \\ 1 & 1 \\ \vdots & \vdots \\ 1 & 1 \end{bmatrix} \begin{bmatrix} s(t+0) \\ -S_{\min} \end{bmatrix} - \begin{bmatrix} \phi_0^{-1}(1-\delta_s) \\ \phi_1^{-1}(1-\delta_s) \\ \phi_2^{-1}(1-\delta_s) \\ \vdots \\ \phi_{N-1}^{-1}(1-\delta_s) \end{bmatrix},$$

where $\phi_{N-1}^{-1}(1-\delta_s)$ is the cumulative distribution function of the random variable $d(t+0)+d(t+1)+d(t+2)+\cdots+d(t+N-1)$.

Remark 2. It is also possible to assume that the behavior of the disturbances can be adjusted as a function of a certain probability distribution. In [27], a normal distribution is used to characterized the behavior of the perturbations, with mean μ and standard deviation σ, i.e., $d(t) = N(\mu,\sigma)$. This assumption could be extended to other patterns or even work directly with historical data, like in this case.

4. Case study and results

In this section, CC-MPC is going to be applied to manage the orders of two drugs available in the hospitals San Juan de Dios and Reina Sofía (both located at Córdoba, Spain). These drugs are not only expensive because of their prices but also because of their maintenance costs, since they must be stored in a fridge. Due to this fact, the reduction of their stock levels is a priority. Due to confidentiality reasons, the specific names and prices of these drugs are going to be omitted.

Regarding the controller, a prediction horizon $N=8$ days has been considered. The evolution of the stock is modeled by using the discrete-time linear model in (14). The orders of these drugs have a minimum amount of 4 units and the maximum has been set to 1000. The prices of the drugs are respectively 227 and 298

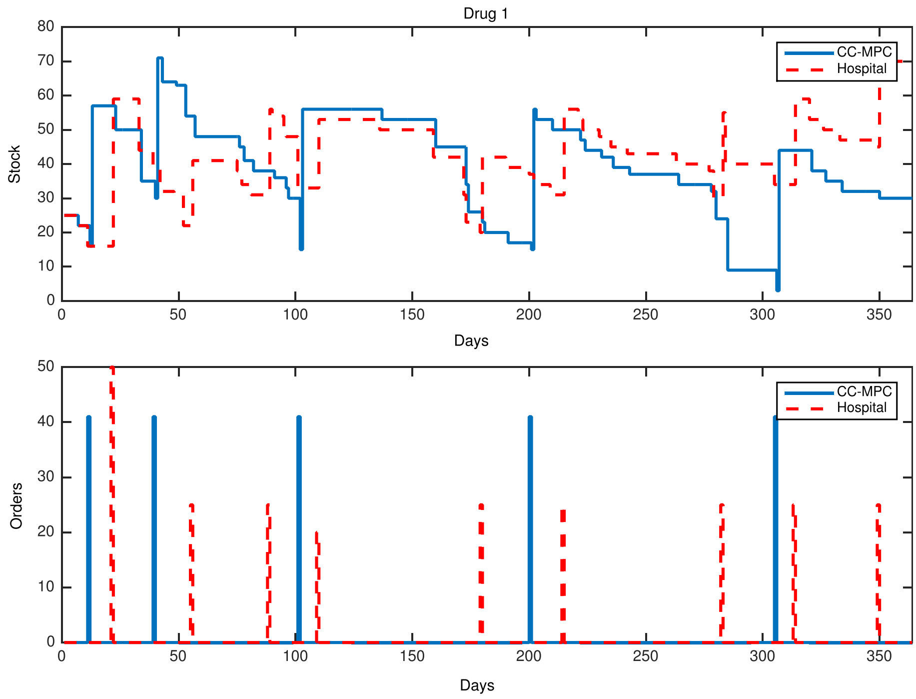

Fig. 2. Real and simulated stock evolution and placed orders for drug 1.

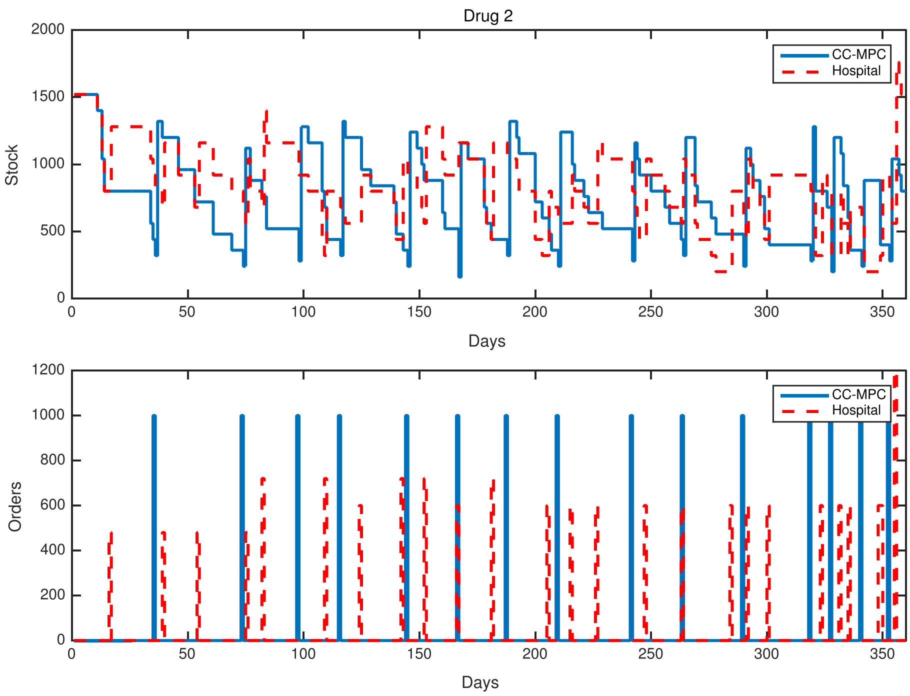

Fig. 3. Real and simulated stock evolution and placed orders for drug 2.

euros per unit, respectively, and each order placed implies an additional cost of 2 euros. The deliveries of these drugs usually have a delay of 2 days with respect to the moment in which the order was placed. The initial values of the stock levels are 500 and 1520, respectively. For simplicity, neither storage cost nor storage limits have been considered at this stage of the proposed work. The only constraint implemented with respect to the stock is that the probability of stockout event has to be lower than 0.001 (i.e., it is requested a reliability level of 99.999 %). Finally, the demand term of (14) is non-deterministic. A probabilistic characterization of their behavior has been calculated for these drugs based on historical data.

If implemented in a hospital, the CC-MPC optimization problem should be solved daily to compute the optimal orders to steer the stock levels as desired. For this simulation, the stock reference (security stock) has been set to 2. All optimization problems were computed by using linear programming routines (`linprog` in *Matlab*) on a machine with an Intel Core 2 Duo CPU with 3.33 GHz and 8 GB RAM. The time needed to calculate the optimal sequence of actions per drug and day was below 10 s. If we take into account

Table 1
Comparison of the behavior of the drug 1 applying CC-MPC and hospital policy.

Approach	Orders	Stock-out	Mean	Desviation
CC-MPC	5	0	39	14
Hospital historical data	9	0	43	11

Table 2
Comparison of the behavior of the drug 2 applying CC-MPC and hospital policy.

Approach	Orders	Stock-out	Mean	Desviation
CC-MPC	15	0	770	316
Hospital historical data	25	0	861	313

that the orders are recomputed once a day, it is possible to calculate optimal control actions for 8640 drugs a day with the current configuration, many more than those used in the hospitals.

The 360-days simulation scenario considered here is shown in Figs. 2 and 3 for each drug. In blue, the evolution of the stocks using CC-MPC is shown. In red, the real evolution of the stock according to the hospital data is shown. Table 4 shows a comparison of the behavior of these two drugs applying CC-MPC with the results registered by the hospitals in this period, considering the average level, standard deviation, and the number of orders. In this period the hospitals placed 9 orders for the drug 1 and 25 for the second one while the CC-MPC policy resulted in 5 and 15 orders respectively. The better timing of the CC-MPC orders and the optimally calculated order size are the key to explain the lower performance of the hospital. On average, the CC-MPC strategy would have resulted in 39 units of drug 1 and 770 of drug 2, i.e., 4 stocked units less of drug 1 and 91 of drug 2 with respect to the results registered by the hospital. Notice also that the CC-MPC strategy results in a slightly greater standard deviation of the stock levels, i.e., the fluctuations in the number of stocked items are a bit bigger with this policy. This is natural since less orders are placed with the CC-MPC strategy. Finally, notice that no stockouts happened during the simulation period (Table 1)

These results clearly show that the CC-MPC policy provides better results than the policy that is currently implemented in the hospital pharmacies. For the first drug, more than 1000 euros on average could be used for purposes other than having stock at the pharmacy with the same clinical results. In the case of drug 2 this amount is 27118 euros. Another noteworthy point is that the staff at the pharmacy department is freed partially from the duties related to the placement and reception of orders. In both cases the CC-MPC placed 40% less orders than the policy followed by the hospital. Finally, note that a more aggressive tuning of the controller could be used to reduce these values at the cost of higher stockout risks (Table 2)

5. Conclusions

Stock management is one of the main tasks of the pharmacy department of a hospital. It is a complex problem due to the uncertainty in the drug demand and the variety of constraints to be considered. In this work, a control technique to deal with this problem has been described and assessed using real data from two Spanish hospitals. The proposed strategy is based on MPC, which allows the fulfillment of the management objectives while taking into account the different operational constraints. The use of chance constraints in combination with MPC makes possible to guarantee the availability of drugs for the patients with a certain level of risk that is explicitly set.

The results of the simulations show that CC-MPC allows reducing the average drug stock level and the work burden in the pharmacy while satisfying the drug demand. The key for the improvement lies on the better time and order size of the proposed approach. Therefore, this control strategy leads to a more efficient use of the resources by the pharmacy department.

Currently, this control approach is translated to C language as a software tool to be implemented in the hospitals that collaborate in this work.

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ARTÍCULOS DE CONGRESO

Capítulo 9

APLICACIÓN DE CONTROL PREDICTIVO ROBUSTO EN GESTIÓN DE INVENTARIOS DE FARMACIA HOSPITALARIA

Application of Robust Model Predictive Control to Inventory Management in Hospitalary Pharmacy

P. Velarde, J. M. Maestre, I. Jurado, I. Fernández, B. Isla Tejera and J. R. del Prado

Abstract— **Inventory management is one of the main tasks that the pharmacy department has to carry out in a hospital. It is a complex problem that requires to establish a tradeoff between different and contradictory optimization criteria. The complexity of the problem is increased due to the constraints that naturally arise in this type of applications. In this paper, which corresponds to preliminary works performed to implement robust and advanced control techniques for pharmacy management in two Spanish hospitals, we propose, assess and compare three robust model predictive control(Chance-Constraints, Multi-Scenarios approach and Tree-Based Methods) as a mean to relieve this issue.**

I. INTRODUCTION

Failures in the stock management in a hospital pharmacy may have catastrophic social and economical consequences. On the one hand, the clinical needs of the hospital have to be satisfied; the social cost of the unavailability of medicines may be enormous as it may lead to the loss of human lives. On the other hand, it is not possible to raise the average stock levels too much. Hospitals have tight budgets that impose constraints on the stock management. In [1] it is estimated that about 35% of hospital expenses on services and goods are due to the pharmacy department. In European countries, where the health care system is public, these expenses are millionaire. Therefore, inventory management is one of the main tasks that a pharmacy department has to carry out in a hospital. It is a complex problem because it requires to establish a tradeoff between contradictory optimization criteria. In addition, other factors that typically complicate inventory management problems have also to be taken into account in this context. For example, there are constraints on the placement of stocked drugs. Room is not endless, specially for those drugs that have to be preserved at low temperature, and thus have to be stored in a fridge. Delays on drug deliveries and non deterministic demands are also major issues in this context.

Typically, the pharmacy managers apply very simple inventory control policies. In particular, an (s, S) policy is usually used, which means that when inventory drops below level s an order is placed to raise it back to S. Alternatively, a fixed size Q can be assigned to the orders and then s is defined as the reorder point. Note that other periodic review inventory control are possible as well, see for example [7] or [2]. Nevertheless, these policies lack of enough flexibility to take into account all the factors involved in this optimization problem in a systematic manner. For this reason, in this work we propose to apply model predictive control (MPC) to the pharmacy department inventory management problem. MPC is a popular control strategy for the design of high performance model-based process control systems because of its ability to handle multi-variable interactions, constraints on control (manipulated) inputs and system states, and optimization requirements in a systematic manner. MPC takes advantage of a system model to predict its future evolution starting from the current system state along a given prediction horizon. Due to its high versatility, MPC has become one of the most popular control techniques in industrial applications [3]. In fact, similar problems such as supply chain management have also benefited from the application of MPC. For example, [8] and [9] applied MPC to supply chain management in semiconductor manufacturing. In [4] a popular supply chain benchmark, the MIT Beer Game, is used to test a distributed MPC algorithm with low communicational burden. Likewise, in [6] robust MPC is applied to production-inventory system. Finally, in [5] a variation of MPC is used to reduce the number of tuning parameters when managing inventories and supply chains.

In the design of predictive controllers for dynamical systems subject to disturbances and/or uncertainty, it is well known that even if the controller finds a feasible solution, there is a certain probability that real outputs may violate the system constraints. Therefore, it would be desirable to replace and/or reformulate the original constraints involving random variables by probabilistic statements, allowing not only the treatment of the uncertainty but also avoiding possible unfeasibility of the optimization problem behind the predictive controller.

In this work, which has been performed in collaboration with two hospitals in Spain, we assess the use of three Robust Model Predictive Control (Chance-Constraints, Multi-scenario approach and Tree-based MPC) to inventory management in Hospitalary Pharmacy, and it is a preliminary work of the project *Pharmacontrol*. The goal of this project is to update the inventory management system of these hospitals so it is possible to reduce the average inventory while maintaining the same clinical guarantees. In order to

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illustrate the size of the problem, it is enough to consider that the biggest hospital that participates in this work has a total capacity of one thousand and two hundred beds for the inpatients. Besides these inpatients, the pharmacy department provides monthly more than five thousand drug dispensations for external patients. In this hospital the expenses on drugs exceed the amount of fifty millions of euros per year.

The paper is organized as follows. First, a description of the inventory management problem is shown in Section II. Section III, presents the optimization problem and the robust techniques MPC for this problem. Section IV some simulations are shown. Finally, in Section V some conclusions are presented.

II. Pharmacy Inventory Problem

In this paper we assume that the pharmacy inventory is composed of N_i different drugs. The following discrete linear model will be used to represent the evolution of the stock level of drug i:

$$s_i(t+1) = s_i(t) + \sum_{j=1}^{np_i} o_i^j(t-\tau_i^j) - d_i(t), \qquad (1)$$

where $s_i \in \mathbb{R}$ is the stock of drug i, $o_i^j \in \mathbb{R}$ is the number of ordered items to the j-th of the np_i providers of the drug i, τ_i^j is its corresponding transport delay, and $d_i(k)$ stands for the aggregate demand of drug i. Note that the number of ordered items can be decomposed as $o_i^j = \delta_i^j(t-\tau_i^j)u_i^j(t-\tau_i^j)$, with $\delta_i^j(t)$ being a boolean variable whose value is one only if an order of drug i to provider j is placed during time t – otherwise its value is zero – and $u_i^j \in \mathbb{R}$ being the actual number of ordered items in case an order is placed. This decomposition is introduced to simplify accounting for costs that are related to the placement of orders.

We consider the following costs associated to the inventory management problem:

- p_i^j is the price that the j-th provider offers for drug i. We will assume for simplicity that this price does not depend on the number of ordered items.
- $C_{sh,i}^j$ is the shipping costs of asking drug i to provider j.
- $C_{op,i}$ represent the costs associated to placing an order of drug i.
- $C_{os,i}$ is the cost of running out of stock of drug i, that is, the cost of shortage. In this case it is possible to ask for help to other hospitals. These loans require to contract special deliveries, which may have a high cost. In addition, the risk of not being able to satisfy the clinical needs of the hospital is maximum at this point.
- $C_{s,i}$ is the cost of storage of drug i.

The goals of a pharmacy manager can be summed up in the following list. Note that the goals are provided in decreasing priority:

1) Demand satisfaction. In other words, the probability of drug shortage has to be minimized. The demand of the drugs is non deterministic. The same may happen with the transport delay associated to the shipments. As a consequence, it is common to set a safety stock in order to cope with the uncertainty introduced by these problems. Two possibilities arise at this point depending on whether a fixed or variable safety stock is set up. In the first case, a minimum bound is introduced in the optimization problem. In the second one, the safety stock becomes an optimization parameter. Anyhow, this is translated into the following mathematical condition:

$$\min_{\delta_i^j, u_i^j \ \forall i,j} \sum_{k=0}^{N} \sum_{i=1}^{N_i} C_{os,i} Pr(s_i(t+k) < 0), \qquad (2)$$

where $Pr(s_i(t+k) < 0)$ stands for the probability of $s_i(t+k)$ being negative and N is the length of the time horizon in which the condition has to be satisfied.

2) Minimize the expenses on the acquisition of drugs and the inventory levels, that is,

$$\min_{\delta_i^j, u_i^j \ \forall i,j} \sum_{k=0}^{N} \sum_{i=1}^{N_i} \sum_{j=1}^{np_i} \delta_i^j(t+k)(p_i^j u_i^j(t+k) + C_{sh,i}^j) + \sum_{k=0}^{N} \sum_{i=1}^{N_i} C_{s,i} s_i(t+k). \qquad (3)$$

3) Minimize the number of orders placed. The human resources of the pharmacy department are limited. Thus, it is convenient to minimize the fixed costs introduced every time an order is placed. This goal is better understood when it is taken into account that, for example, in a hospital such as Reina Sofía more than twelve thousand orders are placed during a year. Mathematically, this condition is equivalent to the following minimization problem:

$$\min_{\delta} \sum_{k=0}^{N} \sum_{i=1}^{N_i} \sum_{j=1}^{np_i} C_{op,i} \delta_i^j(t+k). \qquad (4)$$

In addition, different constraints have to be taken into account:

- **Storage constraints.** On one hand, the stock of drug i has to be greater than a safety stock min_{s_i}, whose mission is to provide an extra guarantee so that the probability of lack of inventory is reduced. On the other, there may be room constraints that limit the maximum number of drug samples that can be stored. Therefore,

$$s_i \in [min_{s_i}, max_{s_i}]. \qquad (5)$$

- **Order constraints.** The constraints on the orders require the use of two different variables. The first one is a boolean variable that represents whether an order of drug i has been placed to provider j during time t. Thus, $\delta_i^j(t) \in [0,1]$. In case of placing an order it has to be taken into account that there is both a minimum and a maximum number of items that can be ordered, that is,

$$u_i^j \in [min_{u_i^j}, max_{u_i^j}]. \qquad (6)$$

- **Operational constraints.** The pharmacy has a limited capacity for placing orders and receiving shipments. For this reason a limit has to be imposed on the number of orders placed during an horizon of length N, that is,

$$\sum_{k=0}^{N}\sum_{j=1}^{np_i}\delta_i^j(t+k)\leq\Delta_i, \tag{7}$$

where Δ_i is the maximum number of orders of drug i that can be placed during the horizon.
- **Economical constraints.** We will consider a constraint on the amount of money that can be spent during the horizon N, being $max_{\$}$ the maximum amount. For simplicity, we will ignore the expenses due to the stocked goods. Thus, this goal can be mathematically translated as:

$$\sum_{k=0}^{N}\sum_{i=1}^{N_i}\sum_{j=1}^{np_i}\delta_i^j(t+k)(p_i^ju_i^j(t+k)+C_{sh,i}^j+C_{op,i}) \leq max_{\$} \tag{8}$$

III. Optimization problem and Model Predictive Control in Pharmacy Inventory

As it was stated in Section II, the objective of the optimization problem is threefold; the demand has to be satisfied, the fixed assets reduced and the number of orders minimized. The system can be represented according to Figure 1.

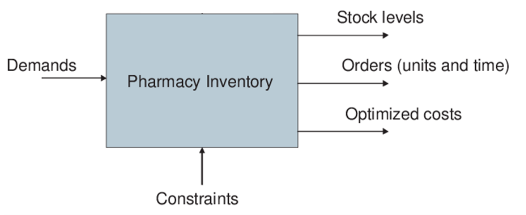

Fig. 1. Block System

System inputs are the estimated drug demands, disturbance and constraints. The outputs are the optimal stock levels, minimum costs and data about when and how many orders should be delivered. The performance index considered in this work involves a multicriteria weighted function where demand satisfaction, expenses and number of orders are included. Note that these terms are defined in Section II as goals of a pharmacy manager, i.e.,

$$\begin{aligned}\min_u J = \beta_1 Dem(u,t) + \beta_2 Expenses(u,t)\\ +\beta_3 Orders(u,t)\end{aligned} \tag{9}$$

where Dem, $Expenses$ and $Orders$ are respectively the terms associated to demand satisfaction, costs and orders. Note that the outputs of the problem depend strongly on the weights β, which prioritizes the different terms.

A. Model Predictive Control

MPC is a control strategy based on the explicit use of a dynamic model to predict the process output at future time instants over a *prediction horizon* (N) [3]. The set of future control signals is calculated by optimizing a criterion or objective function. The predicted outputs depend on the known past inputs and outputs values up to instant k and on the future control signals. Only the control signal calculated for instant k is sent to the process whilst the next control signals are neglected. Some advantages that MPC presents over other optimization control methods include the relative ease of implementation, the ready extension to the multivariable case, and the natural addition of constraints in the optimization.

In this work, MPC has been used to solve the problem. Next, we examine the terms involved in expression (9). The first one is related to the satisfaction of the demand. As it has been said, the demand has a random behavior. Therefore, all we can do is to minimize the probability of drug shortage, as it was shown in expression (2).

B. MPC programming

In the following, we will present some considerations about the inventory control problem in order to ease its implementation. Hence, the objective function will minimize the number of orders placed and the expenses made. Consider the system defined by:

$$s(t+1)=s(t)+o(t-\tau)-d(t), \tag{10}$$

where $s(t)=[s_1(t),...,s_{N_i}(t)]$ is the aggregated stock vector for the np_i different drugs, $d(t)=[d_1(t),...,d_{N_i}(t)]$ is the corresponding demand and $o(t-\tau)=\sum_{j=1}^{np_i}\delta_i^j(t-\tau_i^j)u_i^j(t-\tau_i^j)$ represents the total number of items ordered. As it can be seen, system (10) is equivalent to (1).

The problem to solve is the following:

$$\min_o J$$

subject to (10) and (5)-(8). In this particular problem, we have to deal with two variables of control: a boolean variable $\delta_i^j(t)$ and $u_i^j(t)$, which are components of the control variable $o(t)$. Since finding these two variables together by solving the optimization problem is a difficult task, due to the different nature of them, this problem will be solved by means of an exhaustive search algorithm, solving the problem one time for each possible scenario depending on the value of $\{\delta_i^j(t),...,\delta_i^j(t+N)\}$. With this algorithm, the optimization problem is solved with respect to the variable $u_i^j(t)$.

It is straightforward to see that if $\delta_i^j(t+k)=0, \quad k\in\{0,1,...,N\}$, the number of ordered items $o_i^j(t+k)=0$. Therefore, to simplify the problem, the vector of control variables $\{u_i^j(t),...,u_i^j(t+N)\}$ is reduced eliminating the components $u_i^j(t+k)$ that are multiplied by a $\delta_i^j(t+k)=0$, that is:

$$If\,\delta_i^j(t+k)=0, \quad k\in\{0,1,...,N\},$$

$$\underbrace{\begin{bmatrix} u_i^j(t) \\ \vdots \\ u_i^j(t+k) \\ \vdots \\ u_i^j(t+N) \end{bmatrix}}_{\mathbf{u}_i^j(t)} \rightarrow \underbrace{\begin{bmatrix} u_i^j(t) \\ \vdots \\ u_i^j(t+k-1) \\ u_i^j(t+k+1) \\ \vdots \\ u_i^j(t+N) \end{bmatrix}}_{\mathbf{u'}_i^j(t)},$$

where $\mathbf{u}_i^j(t) \in \mathbb{R}^{N+1}$ and $\mathbf{u'}_i^j(t) \in \mathbb{R}^{N'+1}$, being

$$N' = N - \sum_{k=0}^{N} \left(1 - \delta_i^j(t+k)\right)$$

the number of decision variable. Note that this operation, i.e. to reduce the vector $\mathbf{u}_i^j(t)$ to $\mathbf{u'}_i^j(t)$, can be achieve by means of a simple change of variable:

$$\mathbf{u}_i^j(t) = M\mathbf{u'}_i^j(t),$$

where $M \in \mathbb{R}^{N+1} \times \mathbb{R}^{N'+1}$.

For example, if $N = 4$:

$$\mathbf{u}_i^j(t) = \begin{bmatrix} u_i^j(t) \\ u_i^j(t+1) \\ u_i^j(t+2) \\ u_i^j(t+3) \end{bmatrix},$$

and we are assuming these values: $\delta_i^j(t) = 1$, $\delta_i^j(t+1) = 1$, $\delta_i^j(t+2) = 0$ and $\delta_i^j(t+3) = 1$. That means that the dimension of $\mathbf{u}_i^j(t)$ has to be reduced in one order, so $N' = 3$ and

$$M = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 1 \end{bmatrix},$$

this matrix provides the reduced vector:

$$\mathbf{u'}_i^j(t) = \begin{bmatrix} u_i^j(t) \\ u_i^j(t+1) \\ u_i^j(t+3) \end{bmatrix}.$$

□

Therefore, $\mathbf{u'}_i^j(t)$ contains only the ordered items that are non-zero.

This optimization problem will be solved as many times as possible combinations with the values of $\{\delta_i^j(t), ..., \delta_i^j(t+N)\}$. The optimal combination of $\{\delta_i^j(t), ..., \delta_i^j(t+N)\}$ corresponds with that one that provides the minimal value of the objective function.

It is necessary to pay special attention to the constraints while solving this problem. It is not possible to impose the whole matrix of constraints to the reduced vector $\mathbf{u'}_i^j(t)$, so it is necessary to also apply the change matrix M to the matrix of constraints to impose them only to the control components that we are considering.

C. Chance Constraints MPC

The aggregate demand $d(t)$ has associated a stochastic disturbance, due to the uncertain nature of $d(t)$. As the state is influenced by additive uncertainties $d(t)$, the constraints can not be represented in a deterministic way. Therefore they are rewritten in a probabilistic manner, e.g.:

$$P(s(t+k) \geq s_{min}) \geq 1 - \delta_s, \quad \forall k \in \{1, .., N\},$$

where δ_s is the probability of failure, so it is the risk bound of stockout.

The optimization problem can be written, as:

$$\min_u \mathbf{E}[J], \tag{11}$$

Subject to:

$$s(t+1) = s(t) + o(t-\tau) - d(t) \tag{12}$$

$$P(s_i \in [min_{s_i}, max_{s_i}]) \geq 1 - \delta_s \tag{13}$$

$$u_i^j \in [min_{u_i^j}, max_{u_i^j}]. \tag{14}$$

In addition, considering the constraints (7) and (8).

Developing the expression (13) along the prediction horizon, and assuming that the disturbances behave as a function of a certain probability distribution, it is possible to calculate or estimate the mean and standard deviation of the state variable.

D. Multi-Scenario Approach MPC

To implement the Multi-Scenario technique are not necessary the probabilistic behavior of the demand, it is enough to know several scenarios of possible developments in demand. The calculation of the controller will result in a robust control action to satisfy all the potential disturbances of the extended system, as shown in (15).

$$\begin{bmatrix} s_1(t+1) \\ s_2(t+1) \\ s_3(t+1) \\ \vdots \\ s_K(t+1) \end{bmatrix} = \begin{bmatrix} s_1(t) \\ s_2(t) \\ s_3(t) \\ \vdots \\ s_K(t) \end{bmatrix} + \begin{bmatrix} I \\ I \\ I \\ \vdots \\ I \end{bmatrix} o(t-\tau) - \begin{bmatrix} d_1(t) \\ d_2(t) \\ d_3(t) \\ \vdots \\ d_K(t) \end{bmatrix} \tag{15}$$

Where K is the number of scenarios considered.

In this way, the objective function to be considered is given by (9), subject to (10) and the constraints (5)-(8), replicated for all states of the *extended system.*

E. Tree-Based MPC

This technique consists of modeling the disturbance as a tree, with a number of branches obtained from an initial set of scenarios that represent the dynamics of the disturbances. The reduction of scenarios to a form of trees was performed using the GAMS software. Once reduced the scenes one proceeds to the optimization of the cost function, holds to the own restrictions of the problem, adding restrictions of equality of her actions of control in the points of bifurcation of the disturbances. The system presents it in an extended form for the reduced number of scenarios that are considered, as shown in (16).

$$\begin{bmatrix} s_1(t+1) \\ s_2(t+1) \\ s_3(t+1) \\ \vdots \\ s_R(t+1) \end{bmatrix} = \begin{bmatrix} s_1(t) \\ s_2(t) \\ s_3(t) \\ \vdots \\ s_R(t) \end{bmatrix} + \begin{bmatrix} I & 0 & 0 & \cdots & 0 \\ 0 & I & 0 & \cdots & 0 \\ 0 & 0 & I & \cdots & 0 \\ \vdots & & & \ddots & \vdots \\ 0 & 0 & 0 & \cdots & I \end{bmatrix} o(t-\tau) - \begin{bmatrix} d_1(t) \\ d_2(t) \\ d_3(t) \\ \vdots \\ d_R(t) \end{bmatrix} \quad (16)$$

Where R is the number of reduced scenarios from the initial K scenarios considered. The objective function is given by (9), subject to (10) and the constraints (5)-(8), for each of the possible scenarios based tree.

IV. Case Study and Results

In this section, we apply the proposed robust methods MPC described to one of the most expensives drugs that is used in these hospitals. In addition, this drug deserves special attention since it must be stored in a fridge, which makes even more important to reduce its average stock level. The real name and price of the drug will not be presented in this paper due to confidencialiity reasons.

Regarding the controller, a horizon of 8 days has been considered. The evolution of the stock is modeled using the discrete linear model (10). The orders of this drug have a minimum amount of 4 units and the maximum has been set to 1000. The price of the drug is 250 euros per unit and each order placed implies an additional cost of 2 euros. The deliveries of this drug usually have a delay of 2 days with respect to the moment in which the order was placed. Finally, the demand term of (10) is non deterministic. A probabilistic characterization of its behavior has been calculated for this drug based on historical data from the last seven moths.

A 230 days simulation of the proposed approach is shown in Figures 2, 3 and 4 . In blue, the evolution of the stock using the techniques described above are shown. In red, the real evolution of the stock according to the hospital data is shown. In all cases, the stock was always positive. The characteristics of the results is presented in the table I. Note that, for the price considered, this difference corresponds to an amount of more than 30000 euros that is invested *frozen* unnecesarily. Finally, it is also interesting to notice that during the studied period the hospital placed 26 orders. That is, the applied methods obtained better results even with less orders.

The optimization has to be made taking into account the constraints given by (5-8). A problem is solved at every sampling time to compute a control sequence u that takes the system to the desired reference. For this drug, the stock reference (security stock) has been set to 2.

A word of caution has to be said regarding the results at this point: there may be some uncertainty associated with the real data. Sometimes either the drug dispensations or the arrivals of new items are recorded later than they occurred. Another interesting issue regarding the real evolution is its big peaks, which are usually associated to orders placed before holiday periods (no orders can be placed then). In any

	Orders	Stock-out	Mean	Desviation
Chance- Constraints	13	0	291	101
Multi-scenario	16	0	148	74
Tree-Based	13	0	183	89
Hospital	26	0	394	126

TABLE I

Comparison of the different MPC techniques applied

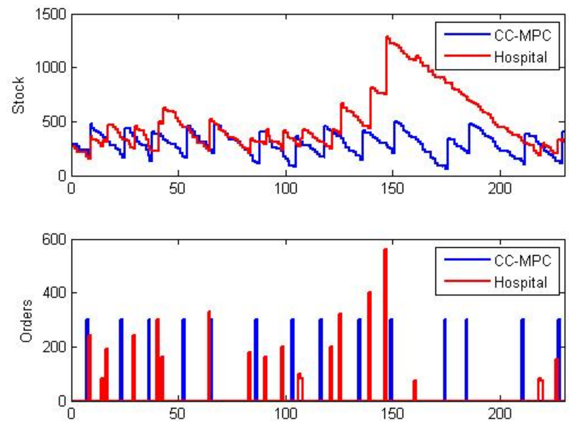

Fig. 2. Real and simulated stock evolution and placed orders applying Chance-Constraints MPC.

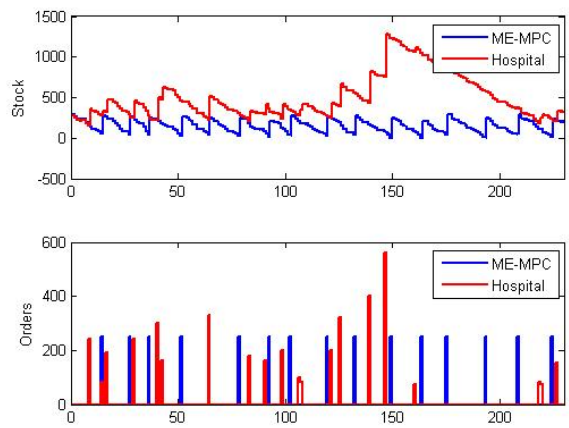

Fig. 3. Real and simulated stock evolution and placed orders applying Multi-scenarios MPC.

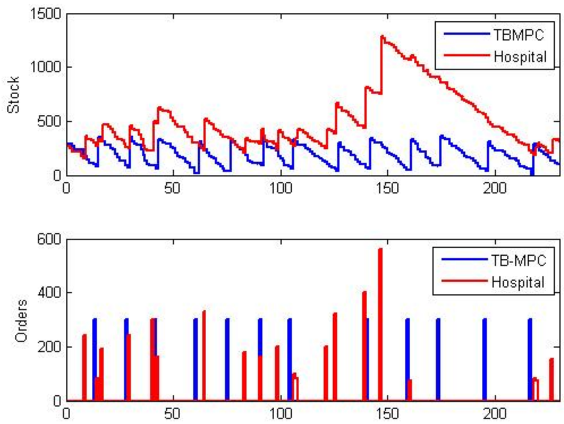

Fig. 4. Real and simulated stock evolution and placed orders applying Tree-Based MPC.

case, the difference between the reality and the simulation is big enough to believe that the application of this kind of policies in this context is promising.

All optimization problems, solved for the exhaustive algorithm, were computed using a linear programming (*linprog* in *Matlab*), on a machine with an Intel Core 2 Duo CPU with 3.33 GHz and 8 GB RAM.

V. Conclusions

As it can be seen, inventory management is one of the main tasks that a pharmacy department has to carry out in a hospital. It is a complex problem that requires to establish a tradeoff between different and contradictory optimization criteria. In this work we have described three control-based methodologies for decision-making in a pharmacy department to address prevention and control problems in the inventory management.

The proposed methodologies optimizes the management of the stock while guaranteeing with a very high probability that the drugs will be available for the patients. In this sense, the MPC framework is particularly useful because of its favorable properties, such as ease of constraint-handling.

Finally, it is worthwhile to mention that the proposed technique may provide important economical savings based on the reduction of the average level of stocked drugs while still guaranteeing the satisfaction of the clinical needs of the hospital. Future work will include the extension of the current framework to consider some of the issues that have not been addressed in this paper and the real implementation of this control policy into the hospitals that collaborate in this project.

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Capítulo 10

OPTIMIZACIÓN DE LA DEMANDA EN FARMACIA HOSPITALARIA

Optimization of the Demand Estimation in Hospital Pharmacy

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Abstract—**Traditionally, the problem of hospital pharmacy management of inventories has been paid little attention. This problem is treated in this paper as a work-in-progress. The main objective is to estimate the demand of stock in different services of the hospital pharmacy, obtaining a reliable method for future planning and management. A better demand estimation implies a better management and therefore, significant savings in inventory costs.**

Some methods will be described an applied to series of data from the *Hospital Universitario Reina Sofía* (Córdoba). The results will be compared in order to establish the best strategy to implement.

I. Introduction

A proper stock management has been always a key point in the business science, because, the storage associated costs have been always a important part of the business costs. Nevertheless, the financial costs associated to the stocks immobilization are the reason for the relevance of stock management techniques in recent times.

These stock management techniques pursue the minimization of the stock costs, while the demand is satisfied without delays ([1], [2], [3], [4]).

The importance of the stock management lies in the fact that it is impossible to acquire immediately the orders in the place and moment that they are needed, in the quantity, quality and minimal price.

In [5], a method to determine the best value for the stock as a function of the risk level and the number of days without stockouts is proposed. The problem addressed in [12] is a comparison of inventory costs and service levels of an in-house three-echelon distribution network vs. an outsourced two-echelon distribution network.

In [13], inventory classification using ABC analysis is used. A simple classification scheme is proposed in this paper using weighed linear optimization.

Inventory management is an important area that is subject to emergency demand situations. A simulation model of a hospital inventory system was developed in [14] to determine the relative significance of several common inventory system variations on a hospital's ability to operate successfully under normal and emergency demand conditions.

In [15], the logistics activities of the hospital pharmacy are optimized. The solution is based on the Just-In-Time (JIT) concept and on an information system that will replace the central hospital pharmacy with a virtual hospital pharmacy, spreading the actual stock of pharmaceuticals in the clinics of all hospitals in the same geographical area.

Nowadays, the costs associated to the stocks are very high; therefore, the main objective is to provide the client in the due date, without accumulating excessive stocks ([5]). In fact, the stocks may represent the 30% of the volume of the business in a company, therefore, small reductions of the stock may suppose a great increase in the benefits. Therefore, a main issue here is to define the amount of existences that, theoretically, should have the company.

In the field of stock management, demand estimation is considered a very important subject, since, it would allow to know the future demand in advance, and that makes possible an efficient stock management. That way, the future demand estimation presents a series of potential benefits, like client service improvement, stock level reduction, personal administration improvement,... Nevertheless, the demand estimation constitutes a critical process in the companies nowadays, because, although there are a lot of statistical methods, they are not used properly, or they are unknown ([6]).

In this paper, the results of a collaboration with the pharmacy service of the *Hospital Universitario Reina Sofía* (Córdoba) are presented. In this case, a proper stock management is fundamental, that is, the patient's needs have to be covered in the most economical way; and a fundamental tool for a proper stock management is the demand estimation.

Therefore, this paper is a work-in-progress which objective is to optimize the demand estimation of the drugs for the external patients ([7]), which are the main source of certain drugs demand. To do that, different prediction methods are applied to the historical data series, and the most appropriate method is determined for each case, optimizing the demand estimation.

This paper is organized as follows: Section II describes the prediction method to applied. Section III presents a method

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used for stock analysis. In Section IV some results are shown. Finally, in Section V some conclusions and future work are presented.

II. Methods for demand estimation

In this section, different quantitative techniques are presented ([8]). They can be classified in two types:

- **Temporal series.**
- **Causal models.**

These quantitative techniques are described in the subsequent sections.

A. *Quantitative model: Temporal series*

These prediction models are based in historical data of a variable, the history is analyzed to discover patterns like tendency, seasonality or cycles, the obtained patterns are projected to the future. As these patterns are not valid for long periods of time, these models are essentially useful to predict medium and short-term ([9]).

In the following, the quantitative prediction models are theoretically described.

Simple approach

The simplest estimation for the period $n+1$ consists in the assumption that the process is changing very slowly and that the value of the variables does not change from one period to another:

$$\hat{Y}_{n+1} = Y_n, \quad n+1 \geq 2, \tag{1}$$

where Y_n is the variable under consideration, in this case the demand, in period n and $\hat{Y}_{n+1}$ is the estimation of that variable for the period $n+1$.

It is straightforward to see that this method does not consider variations due to seasons or cycles, and overestimates the random variations. Furthermore, it has the disadvantage of being imprecise due to its large variance. Nevertheless, it is recommended when the series' information in times before t is meaningless, that is, its use has been invalidated, or simply the information does not exist, or it can be used as a starting point to more sophisticated methods, being the technique with the best efficiency-cost rate ([8]).

Simple moving mean

This prediction method uses just the last n periods, and the next expression:

$$\hat{Y}_{n+1} = \sum_{i=t-n+1}^{t} (Y_i)/n \tag{2}$$

This technique does not only use all the relevant data from the last n periods, but also the actualization between periods is done easily, eliminating the first observation and aggregating the last one.

One advantage of this procedure is that the calculations are very simple and, however, the system is flexible, considering that the tendency is not forced to fit a particular math function.

The moving mean behavior depends on n, if the value of n is large, the moving mean responds slowly to effective changes; on the other hand, if the value of n is small, the response is quicker ([8]).

Exponential smoothing

The basic idea is that it is possible to calculate a prediction from a previous mean, the most recent demand and a smoothness constant α.

The expression for the estimation for the period $n+1$ is:

$$\hat{Y}_{n+1} = \alpha Y_n + (1-\alpha)\hat{Y}_n, \quad n \geq 1, \tag{3}$$

where the value $\hat{Y}_1$ represents the estimation for the first historical period, using typically $\hat{Y}_1 = Y_1$. Furthermore, the smoothness constant $\alpha \in (0,1)$ is incorporated, that allows to decrease the influence of distant values, diminishing importance to a proper choice of $\hat{Y}_1$. To do that, n weights α_i are defined, obtained from the parameter α, according to the geometric progression with ratio $q = 1\alpha$, with $\alpha_i = \alpha$.

The estimation is done depending on the real value, and the estimation, obtained in the last period, although the n values of Y are considered implicitly.

If large values are chosen for α, more weight is given to real recent values, while, choosing small values for α, bigger weights are reserved for substantial changes in the behavior of the variable under study, that way, the model responds quicker to changes in the demand.

This method is recommended when the temporal horizon of the prediction is short, no information about any independent factor that affects the demand is known, there are not too much resources and efforts to invert in the prediction and it is desired that the prediction can follow the tendencies and the seasonality ([8]).

Box-Jenkins: ARIMA

They are more complex statistical models. The more general one is the ARIMA model, an integrated auto-regressive model with mobile mean, that consists in identify a possible prediction model, estimate its parameters and determine its goodness ([10], [11]).

The main advantage of these models is that they provide optimal predictions in short-term, due to Box-Jenkins methodology allows to choose between a wide range of models, depending on how they represent the data series behavior. Nevertheless, determinate the model that fits best the data series is not trivial, and wide knowledge is required about this methodology.

The ARIMA models are built from ARMA models. The ARMA model typical expression (p,q) is the following:

$$\begin{aligned} Y_t = C + &\underbrace{\phi_1 \times Y_{t-1} + \cdots + \phi_p \times Y_{t-p}}_{\text{Auto-regressive comp.}} \\ + &\underbrace{\theta_1 \times \epsilon_{t-1} + \cdots + \theta_q \times \epsilon_{t-q}}_{\text{Mobile mean comp.}} + \epsilon_t, \end{aligned} \tag{4}$$

where the variable that defines the temporal series Y_t depends on a constant C, on the past values of the same variables (auto-regressive component AR) and on the error past values (mobile mean component MA).

The number of delays in the temporal series that are introduced in the model are denominated auto-regressive order of the model and it is denoted p. While the number of past errors introduced in the model is denominated mobile mean order of the model, and it is denoted by q.

Therefore, an ARIMA model (p,d,q) is an ARMA model (p,q) of the d times differentiated series. And its typical expression is the following:

$$\begin{aligned} Y_t^{(d)} &= C + \underbrace{\phi_1 \times Y_{t-1}^{(d)} + \cdots + \phi_p \times Y_{t-p}^{(d)}}_{\text{Auto-regressive comp.}} \\ &+ \underbrace{\theta_1 \times \epsilon_{t-1}^{(d)} + \cdots + \theta_q \times \epsilon_{t-q}^{(d)}}_{\text{Mobile mean comp.}} + \epsilon_t^{(d)}, \end{aligned} \quad (5)$$

where $Y_t^{(d)}$ is the differences series of order d and $\epsilon_t^{(d)}$ is the error series committed in the last series.

The ARIMA model can be defined as a multiple linear regressive model, where the dependent variable is the series itself, differentiated or not, and the independent variables are series values and error values delayed to orders p and q, respectively. In fact, once the model has been identified, the parameters $p+q$ determination is done in the same way that in the case of multiple regression, that is, by means the minimization of the quadratic error.

B. Quantitative model: Causal model

In general, causal prediction methods assume that exit a cause-effect relation between a dependent variable (demand), and other independent variables ([8]). There exist a lot of methods, now, the most famous is presented.

Simple linear regression

A linear relation between the variable to predict (dependent variable), and other variable (independent variable), is assumed. This relation can be represented mathematically as follows:

$$\hat{Y}_i = a + bX_i \quad i = 1, 2, \ldots, n, \quad (6)$$

where $\hat{Y}$ is the estimated demand (depend variable) and X is the period of time between the visits of the patient (independent variable).

Taking into account that usually, the observations are widely disperse, the best technique to determine the values a and b is the minimum squares method.

This method is based in the idea of minimizing the distant between real observations Y, and corresponding points estimated by means the regression straight line $\hat{Y}$. Concretely, the values a and b are determined in such a way the sum of the squares of the errors is minimized, between the real value Y, and the estimated one $\hat{Y}$.

Multiple linear regression

This method is used to study the relation between a dependent variable and various independent variables, being the generic form of this model the following:

$$\begin{aligned} &\hat{Y}_i = a_1 X_{i1} + a_2 X_{i2} + \ldots + a_k X_{ik} \\ &i = 1, 2, \ldots, n, \end{aligned} \quad (7)$$

where $\hat{Y}$ is the dependent variable, X_{i1}, X_{i2}, ... , X_{ik}, are the independent variables, and the i subscript indicates the n sampled observations.

The same idea of minimal squares used in the case of the simple linear regression can be used in this case to estimate the best values of a_1, a_2, ... , a_k.

One of the most important characteristics of causal models is that they can be used to predict changing points in the demand function. In contrast, the time series models can be used to predict the pattern of future demand taking as basis the historical data, but these models can not predict high and low points in demand levels.

Due to its capacity to predict changing points, the causal models are generally exacter than time series models to formulate medium and long-term predictions.

III. Stock analysis

In this section, a method to deal with the different items in the store of the pharmacy is presented. With this method, it will be possible to classified the different drugs depending on its importance, price,... This will be useful in order to know which drugs require more attention and accuracy in their demand estimation.

A. ABC criteria

In general, in the storehouse of any company, it is usual to find a large number of items with different characteristics. It is obvious to think that all of these items do not represent the same volume of immobilized capital, and they are not equally important for the company's behavior.

Taking that into account, it is natural to conclude that the technique procedure and the control to apply in the stock management of the items' storehouse of a company do not have to be equal for all of them. It will be necessary to pay more attention and to be more precise in the management of those items that, because of its price, represent a higher percentage of the existences investment.

To do that, the items have been classified taking into account just the immobilized percentage that they represent respect to the total immobilized existences. The items have been classified in three categories: A, B and C, denominating this classification procedure as ABC method. In the A group are included the items that, although they represent a small percentage in physical units respect to the total items, they are the highest part of the immobilized capital of the stock. In the B group are included those with second order in value. And in the C group are included those items that, although they represent a high percentage in physical units respect to the total, they suppose a small percentage of the immobilized capital.

The item classification depending on their value has, in general, a similar distribution to the Pareto's one: about a 20% of the number of items in stock represent almost an 80% of the total value of the stock, as shown in Fig. 1.

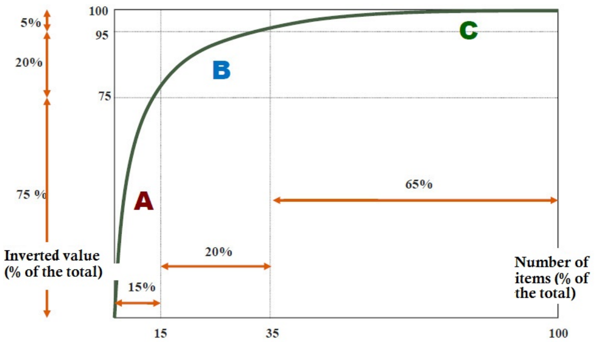


Fig. 1. ABC classification of the stock objects.

This way, in the pharmacy service of the *Hospital Universitario Reina Sofía* (Córdoba), the ABC criteria is applied to the stock, and they select 10 drugs with high financial value percentage and maximum utility, where it is necessary to focus attention, surveillance and preciseness in the computations.

IV. Practical application of prediction methods

In this section, the presented prediction method are going to be applied using the historical data from the pharmacy service of the *Hospital Universitario Reina Sofía* (Córdoba). After that, the applied prediction methods are going to be compared y the most appropriate for each case is going to be determined.

All these prediction methods are going to be compared also with the procedure that the hospital is using nowadays, that is, basing the estimation on the mean consumption in the last 12 months, independently of the drug under consideration.

To do that, all these techniques are going to be applied on 10 different drugs. The tuning parameters for each strategy are chosen by applying an iterative method and the data historical is equal to 28 weeks.

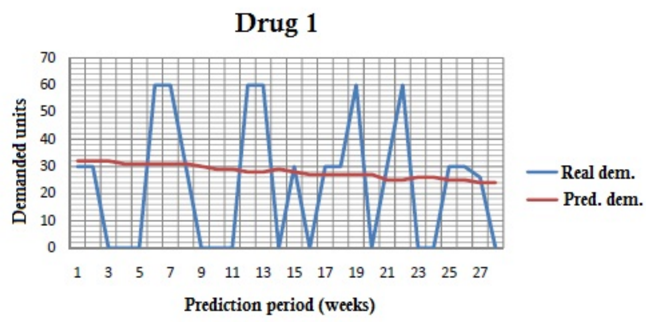
In order to show the behavior of the different techniques, the results for drug 1 are presented in Fig. 2, 3, 4, 5, 6, 7 and 8.

Fig. 2 shows how the hospital procedure provides a predicted demand that adapts reasonably well the mean of the real demand. This method in particular uses a data historical of 52 weeks.

In Fig. 3, it can be seen how the method just delay the real demand to obtain the predicted one.

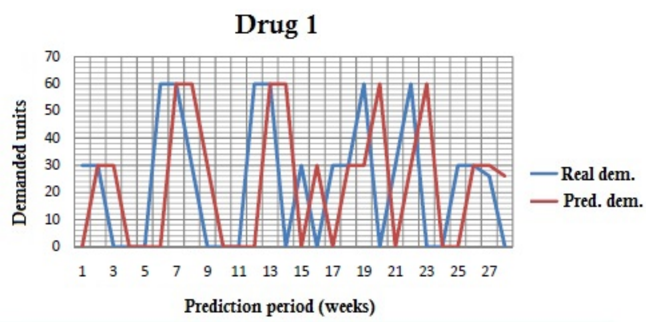
Fig. 4 and 5 also adapt reasonably well the predicted demand to the mean of the real demand.

In Fig. 6, it can be seen how the demand is not as well estimated to the mean of the real demand as in the previous figures.



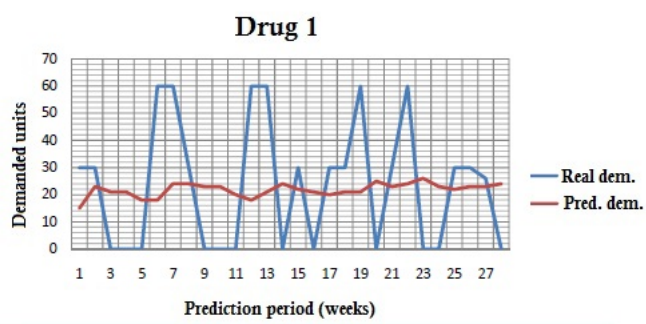
MEAN ERROR	MEAN ABSOLUTE ERROR	TYPICAL DEVIATION
-4,68	20,04	23,37

Fig. 2. Hospital procedure



MEAN ERROR	MEAN ABSOLUTE ERROR	TYPICAL DEVIATION
0,00	23,57	31,96

Fig. 3. Simple approach



MEAN ERROR	MEAN ABSOLUTE ERROR	TYPICAL DEVIATION
1,61	20,82	23,83

Fig. 4. Simple moving mean

Fig. 7 and 8 show how that methods try to follow the real evolution of the demand although the mean is not estimated as well as before.

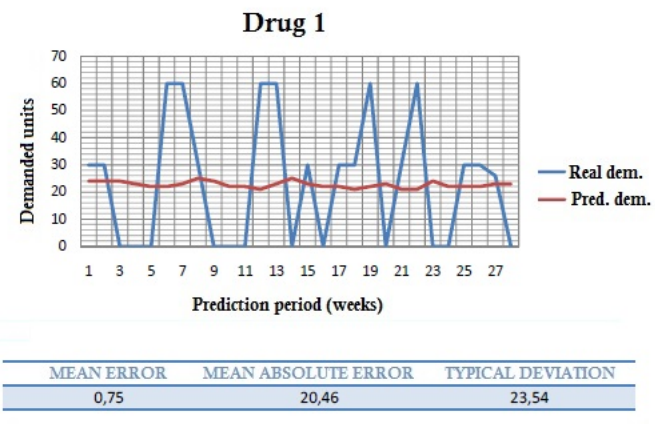


Fig. 5. Exponential smoothing

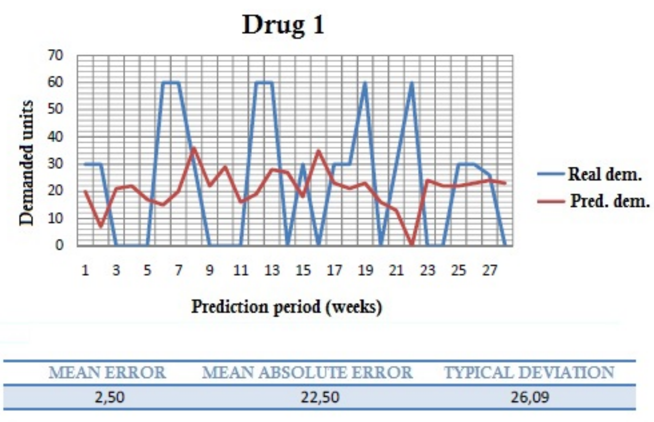


Fig. 6. ARIMA

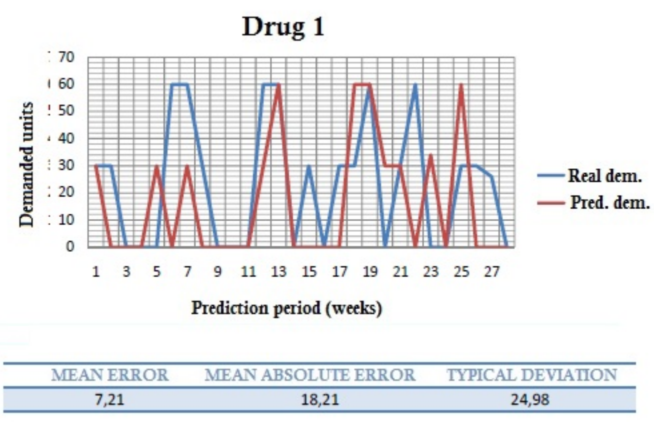


Fig. 7. Simple linear regression

All of these graphics were obtained also for the remaining 9 drugs.

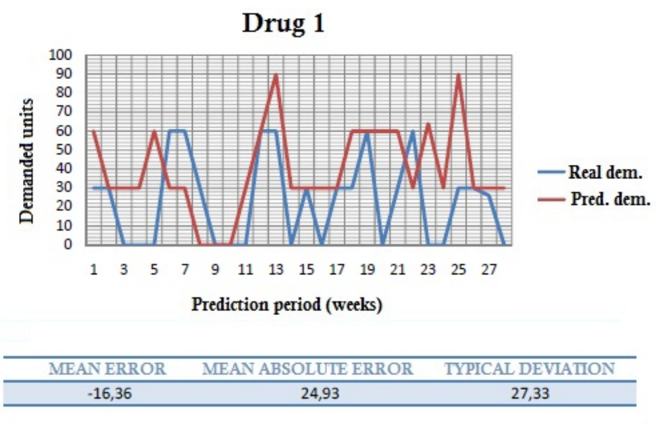


Fig. 8. Multiple linear regression

TABLE I. TIMES OF OPTIMALITY FOR EACH METHOD

Prediction method	Times of opt.
Hospital	5
Simple approach	0
Simple moving mean	1
Exponential smoothing	1
ARIMA	1
Simple linear regression	2
Multiple linear regression	0

In this paper, three error measurement are available: the mean error, the mean absolute error and the typical deviation. Taking that values into account, a methodology for comparison is described.

This methodology represents, for each drug, a dispersion of points. These points represent the prediction methods. For a specific case, the mean absolute error is represented in the x axis while the typical deviation is represented in the y axis. This is repeated for each method.

The optimal method is the one with the closest representation to the point $(0, 0)$.

This representation is shown in Fig. 9 for drug 1. This figure shows that the optimal procedure for the drug 1 is the one used by the hospital.

Table I shows how many times is optimal each prediction method (for the 10 drugs).

As can be seen from the results, no method is optimal for all the cases.

For the 10 drugs under study, the simple moving mean, the exponential smoothing and the ARIMA method provide the best estimation for 1 drug each one. The simple linear regression causal model is optimal for 2 drugs. And finally, the method used by the hospital provides the best estimation for 5 drugs.

The reason for this result could be that the data historical for the method used by the hospital is greater than the one

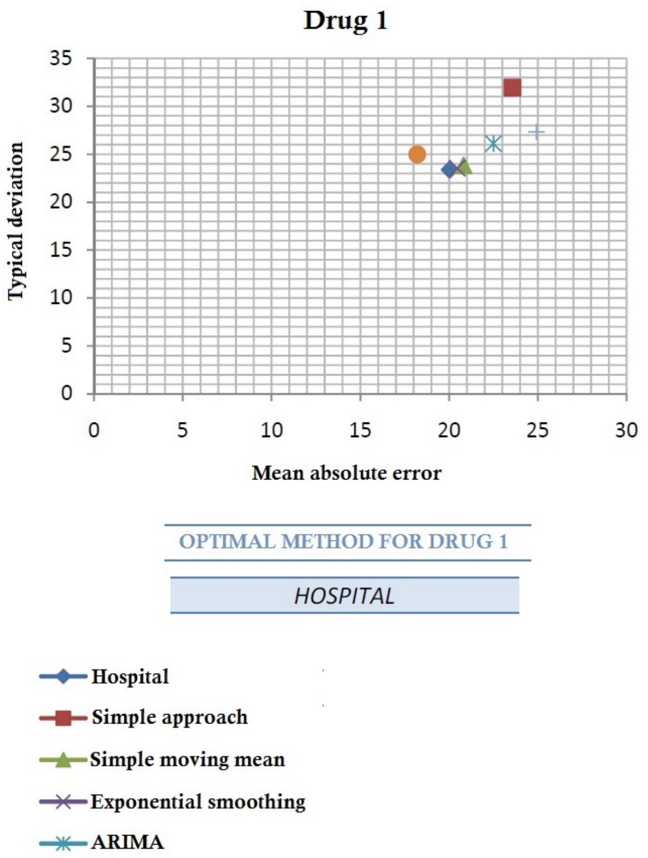


Fig. 9.

for all the other methods. That fact could act in favor of the winning method.

V. Conclusions and future work

This paper has presented some techniques to predict the demand of drugs in the pharmacy service of a hospital.

From the results, it can be concluded that there is no a unique method that provide optimal results for the estimation for any drug. The best thing that the hospital could do in this situation would be a dynamical analysis of the data and to choose the best procedure for each case.

As this paper has been a work-in-progress, there are many lines to follow as future work. The first one would be to add a stage of pre-processing data. Also, the data historical could be augmented, in order to evaluate all the method in equal conditions.

It would be very useful as well, to investigate new prediction method, as neuronal networks.

Finally, the study could be extended to a larger number of drugs.

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Capítulo 11

UNA APLICACIÓN DE CONTROL PREDICTVO CON RESTRICCIONES DE PROBABILIDAD A GESTIÓN DE INVENTARIOS EN FARMACIA HOSPITALARIA

An Application of Chance-Constrained Model Predictive Control to Inventory Management in Hospitalary Pharmacy

J. M. Maestre, P. Velarde, I. Jurado, C. Ocampo-Martínez, I. Fernández, B. Isla Tejera and J. R. del Prado

***Abstract*— Inventory management is one of the main tasks that the pharmacy department has to carry out in a hospital. It is a complex problem that requires to establish a tradeoff between different and contradictory optimization criteria. The complexity of the problem is increased due to the constraints that naturally arise in this type of applications. In this paper, which corresponds to preliminary works performed to implement advanced control techniques for pharmacy management in two Spanish hospitals, we propose and assess chance-constrained model predictive control (CC-MPC) as a mean to relieve this issue.**

I. INTRODUCTION

Inventory control is a classical problem that arises in many fields. Wherever there is an organization that provides a certain good or service, there is a need of controlling the items that are bought to this end. Ideally, the organization would know exactly when these items will be needed, and hence they could be ordered to arrive and be used just in time. Unfortunately, this is not realistic due to the existing uncertainties with respect to the demand and material or information delays. As a consequence, some conservatism in the control policy used is necessary in order to avoid stockouts, specially because the consequences of such event can be fatal.

Failures in the stock management in a hospital pharmacy may have catastrophic social and economical consequences. On the one hand, the clinical needs of the hospital have to be satisfied; the social cost of the unavailability of medicines may be enormous as it may lead to the loss of human lives. On the other hand, it is not possible to raise the average stock levels too much. Hospitals have tight budgets that impose constraints on the stock management. In [1] it is estimated that about 35% of hospital expenses on services and goods are due to the pharmacy department. In European countries, where the health care system is public, these expenses are millionaire. Therefore, inventory management is one of the main tasks that a pharmacy department has to carry out in a hospital. It is a complex problem because it requires to establish a tradeoff between contradictory optimization criteria. In addition, other factors that typically complicate inventory management problems have also to be taken into account in this context. For example, there are constraints on the placement of stocked drugs. Room is not endless, specially for those drugs that have to be preserved at low temperature, and thus have to be stored in a fridge. Delays on drug deliveries and non deterministic demands are also major issues in this context.

Typically, the pharmacy managers apply very simple inventory control policies. In particular, an (s, S) policy is usually used, which means that when inventory drops below level s an order is placed to raise it back to the inventory higher level S. Alternatively, a fixed size Q can be assigned to the orders and then s is defined as the reorder point. Note that other periodic review inventory control are possible as well, see for example [12] or [2]. Nevertheless, these policies lack of enough flexibility to take into account all the factors involved in this optimization problem in a systematic manner. For this reason, in this work we propose to apply model predictive control (MPC) to the pharmacy department inventory management problem. MPC is a popular control strategy for the design of high performance model-based process control systems because of its ability to handle multivariable interactions, constraints on control (manipulated) inputs and system states, and optimization requirements in a systematic manner. MPC takes advantage of a system model to predict its future evolution starting from the current system state along a given prediction horizon. Due to its high versatility, MPC has become one of the most popular control techniques in industrial applications [3]. In fact, similar problems such as supply chain management have also benefited from the application of MPC. For example, [13] and [14] applied MPC to supply chain management in semiconductor manufacturing. In [7] a popular supply chain benchmark, the MIT Beer Game, is used to test a distributed MPC algorithm with low communicational burden. Likewise, in [11] robust MPC is applied to production-inventory system. Finally, in [9] a variation of MPC is used to reduce the number of tuning parameters when managing inventories and supply chains.

In the design of predictive controllers for dynamical systems subject to disturbances and/or uncertainty, it is well known that even if the controller finds a feasible solution, there is a certain probability that real outputs may violate the system constraints. Therefore, it would be suitable to replace

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and/or reformulate the original constraints involving random variables by probabilistic statements, allowing not only the treatment of the uncertainty but also avoiding possible unfeasibility of the optimization problem behind the predictive controller. Probabilistic or chance constraints, which have been treated and developed within the stochastic programming framework [6], were firstly introduced during the 60s - 70s [8]. Combined with the standard MPC theory, they allow the designer to arise with a stochastic optimization problem behind the controller by replacing hard constraints (either of states or inputs) with probabilistic constraints and by replacing the nominal cost function with its expected value in the MPC formulation [4]. This stochastic approach, known as Chance-Constrained MPC (CC-MPC) demonstrates to be suitable for large-scale complex systems due to its inherent features such as robustness, flexibility, low computational requirements, and ability to include the level of reliability (or risk) associated with the constraints (which implies its a priori knowledge) [10], [5]. Thus, CC-MPC avoids the conservative nature of other MPC approaches taking into account the expected performance of the closed loop with proper constraint handling instead of directly trying to assure robust stability.

In this work, which has been performed in collaboration with two hospitals in Spain, we assess the use of CC-MPC to inventory management in Hospitalary Pharmacy, and it is a preliminary work of the project *Pharmacontrol*[1]. The goal of this collaboration is to update the inventory management system of these hospitals so it is possible to reduce the average inventory while maintaining the same clinical guarantees. In order to illustrate the size of the problem, we will say that the biggest hospital that participates in this work has a total capacity of 1200 beds for the inpatients. Besides these inpatients, the pharmacy department provides monthly more than five thousand drug dispensations for external patients. In this hospital the expenses on drugs exceed the amount of fifty millions of euros per year.

The paper is organized as follows. First, a description of the inventory management problem is shown in Section II. Section III, presents the optimization problem and the MPC for this problem. Section IV some simulations are shown. Finally, in Section V some conclusions are presented.

II. Pharmacy Inventory Problem

In this paper we assume that the pharmacy inventory is composed of N_i different drugs. The following discrete linear model will be used to represent the evolution of the stock level of drug i:

$$s_i(t+1) = s_i(t) + \sum_{j=1}^{n_{p_i}} o_i^j(t-\tau_i^j) - d_i(t), \qquad (1)$$

where $s_i \in \mathbb{R}$ is the stock of drug i, $o_i^j \in \mathbb{R}$ is the number of ordered items to the j-th of the n_{p_i} providers of the drug i, τ_i^j is its corresponding transport delay, and $d_i(k)$ stands for the aggregate demand of drug i. Note that the number of ordered items can be decomposed as $o_i^j = \delta_i^j(t-\tau_i^j)u_i^j(t-\tau_i^j)$, with $\delta_i^j(t)$ being a boolean variable whose value is one only if an order of drug i to provider j is placed during time t – otherwise its value is zero – and $u_i^j \in \mathbb{R}$ being the actual number of ordered items in case an order is placed. This decomposition is introduced to simplify accounting for costs that are related to the placement of orders.

[1]The project *Pharmacontrol* has as main objective the improvement of the stock control in hospital pharmacies, trying to reduce the stock mean level and, therefore, achieving considerable savings for the hospitals.

We consider the following costs associated to the inventory management problem:

- p_i^j is the price that the j-th provider offers for drug i. This price could depend in general on the number of ordered items. On way to proceed in that case would be to estimate that dependency (adjusting with an expression that could be linear, quadratic, ...) to include explicitly in this term the decision variable o_i^j. We will assume for simplicity that this price does not depend on the number of ordered items.
- $C_{sh,i}^j$ is the shipping costs of asking drug i to provider j.
- $C_{op,i}$ represent the costs associated to placing an order of drug i.
- $C_{os,i}$ is the cost of running out of stock of drug i, that is, the cost of shortage. In this case it is possible to ask for help to other hospitals. These loans require to contract special deliveries, which may have a high cost. In addition, the risk of not being able to satisfy the clinical needs of the hospital is maximum at this point.
- $C_{s,i}$ is the cost of storage of drug i.

The goals of a pharmacy manager can be summed up in the following list. Note that the goals are provided in decreasing priority:

1) Demand satisfaction. In other words, the probability of drug shortage has to be minimized. The demand of the drugs is non deterministic. The same may happen with the transport delay associated to the shipments. As a consequence, it is common to set a safety stock in order to cope with the uncertainty introduced by these problems. Two possibilities arise at this point depending on whether a fixed or variable safety stock is set up. In the first case, a minimum bound is introduced in the optimization problem. In the second one, the safety stock becomes an optimization parameter. Anyhow, this is translated into the following mathematical condition:

$$\min_{\delta_i^j, u_i^j\ \forall i,j} \sum_{k=0}^{N} \sum_{i=1}^{N_i} C_{os,i} Pr(s_i(t+k) < 0), \qquad (2)$$

where $Pr(s_i(t+k) < 0)$ stands for the probability of $s_i(t+k)$ being negative and N is the length of the time horizon in which the condition has to be satisfied.
2) Minimize the expenses on the acquisition of drugs and

the inventory levels, that is,

$$\min_{\delta_i^j, u_i^j \ \forall i,j} \sum_{k=0}^{N} \sum_{i=1}^{N_i} \sum_{j=1}^{n_{p_i}} \delta_i^j(t+k)(p_i^j u_i^j(t+k) + C_{sh,i}^j) + \sum_{k=0}^{N} \sum_{i=1}^{N_i} C_{s,i} s_i(t+k). \tag{3}$$

3) Minimize the number of orders placed. The human resources of the pharmacy department are limited. Thus, it is convenient to minimize the fixed costs introduced every time an order is placed. This goal is better understood when it is taken into account that, for example, in a hospital such as Reina Sofía more than twelve thousand orders are placed during a year. Mathematically, this condition is equivalent to the following minimization problem:

$$\min_{\delta} \sum_{k=0}^{N} \sum_{i=1}^{N_i} \sum_{j=1}^{n_{p_i}} C_{op,i} \delta_i^j(t+k). \tag{4}$$

In addition, different constraints have to be taken into account:

- **Storage constraints.** On one hand, the stock of drug i has to be greater than a safety stock $s_{i,min}$, whose mission is to provide an extra guarantee so that the probability of lack of inventory is reduced. On the other, there may be room constraints that limit the maximum number of drug samples that can be stored. Therefore,

$$s_i \in [s_{i,min}, s_{i,max}]. \tag{5}$$

- **Order constraints.** The constraints on the orders require the use of two different variables. The first one is a boolean variable that represents whether an order of drug i has been placed to provider j during time t. Thus, $\delta_i^j(t) \in [0, 1]$. In case of placing an order it has to be taken into account that there is both a minimum and a maximum number of items that can be ordered, that is,

$$u_i^j \in [u_{i,min}^j, u_{i,max}^j]. \tag{6}$$

- **Operational constraints.** The pharmacy has a limited capacity for placing orders and receiving shipments. For this reason a limit has to be imposed on the number of orders placed during an horizon of length N, that is,

$$\sum_{k=0}^{N} \sum_{j=1}^{n_{p_i}} \delta_i^j(t+k) \leq \Delta_i, \tag{7}$$

where Δ_i is the maximum number of orders of drug i that can be placed during the horizon.

- **Economical constraints.** We will consider a constraint on the amount of money that can be spent during the horizon N, being $\$_{max}$ the maximum amount. For simplicity, we will ignore the expenses due to the stocked goods. Thus, this goal can be mathematically translated as:

$$\sum_{k=0}^{N} \sum_{i=1}^{N_i} \sum_{j=1}^{n_{p_i}} \delta_i^j(t+k)(p_i^j u_i^j(t+k) + C_{sh,i}^j + C_{op,i}) \leq \$_{max} \tag{8}$$

III. Optimization problem and Model Predictive Control in Pharmacy Inventory

As it was stated in Section II, the objective of the optimization problem is threefold; the demand has to be satisfied, the fixed assets reduced and the number of orders minimized. The system can be represented according to Figure 1.

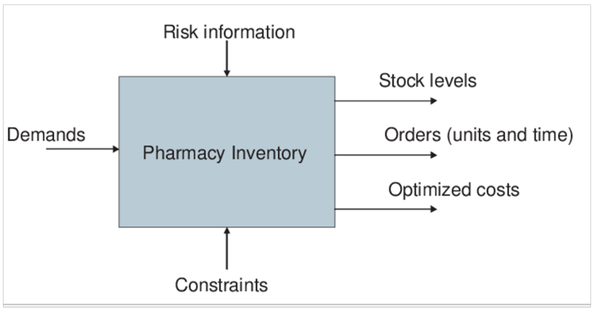

Fig. 1. Block System

System inputs are the estimated drug demands, disturbance and constraints. The outputs are the optimal stock levels, minimum costs and data about when and how many orders should be delivered. The performance index considered in this work involves a multicriteria weighted function where demand satisfaction, expenses and number of orders are included. Note that these terms are defined in Section II as goals of a pharmacy manager, i.e.,

$$\min_{u} J, \tag{9}$$

$$\text{with} \quad J = \beta_1 \Delta(u,t) + \beta_2 E(u,t) + \beta_3 \Theta(u,t),$$

where Δ, E and Θ are respectively the terms associated to demand satisfaction, costs and orders. Note that the outputs of the problem depend strongly on the weights β, prioritizing the different terms. These parameters are chosen following the recommendations of the hospital.

At the end, the problem to solve is a deterministic one, with the particularity that the constraints are obtained from probabilistic assumptions.

A. Model Predictive Control

MPC is a control strategy based on the explicit use of a dynamic model to predict the process output at future time instants over a *prediction horizon* (N) [3]. The set of future control signals is calculated by optimizing a criterion or objective function. The predicted outputs depend on the known past inputs and outputs values up to instant k and on the future control signals. Only the control signal calculated for instant k is sent to the process whilst the next control signals are neglected. Some advantages that MPC presents over other optimization control methods include the relative ease of implementation, the ready extension to the multivariable case, and the natural addition of constraints in the optimization.

In this work, MPC technique has been used to solve the problem. Next, we examine the terms involved in expression (9). The first one is related to the satisfaction of the demand. As it has been said, the demand has a random behavior. Therefore, all we can do is to minimize the probability of drug shortage, as it was shown in expression (2).

B. MPC programming

In the following, we will present some considerations about the inventory control problem in order to ease its implementation. Hence, the objective function will minimize the number of orders placed and the expenses made. Consider the system defined by:

$$s(t+1) = s(t) + o(t-\tau) - d(t), \qquad (10)$$

where $s(t) = [s_1(t), ..., s_{N_i}(t)]$, $d(t) = [d_1(t), ..., d_{N_i}(t)]$ and $o(t-\tau) = \sum_{j=1}^{n_{p_i}} \delta_i^j(t-\tau_i^j) u_i^j(t-\tau_i^j)$ represents the total number of items ordered. As it can be seen, system (10) is equivalent to (1).

The problem to solve is the following:

$$\min_{o} J$$

subject to (10) and (5)-(8). In this particular problem, we have to deal with two variables of control: a boolean variable $\delta_i^j(t)$ and $u_i^j(t)$, which are components of the control variable $o(t)$. Since finding these two variables together solving the optimization problem is a difficult task, due to the different nature of them, this problem will be solved by means of an exhaustive search algorithm, solving the problem one time for each possible scenario depending on the value of $\{\delta_i^j(t), ..., \delta_i^j(t+N)\}$. With this algorithm, the optimization problem is solved with respect to the variable $u_i^j(t)$.

It is straightforward to see that if $\delta_i^j(t+k) = 0, \quad k \in \{0, 1, ..., N\}$, the number of ordered items $o_i^j(t+k) = 0$. Therefore, to simplify the problem, the vector of control variables $\{u_i^j(t), ..., u_i^j(t+N)\}$ is reduced eliminating the null component $u_i^j(t+k)$, that is:

$$\forall \delta_i^j(t+k) = 0, \quad k \in \{0, 1, ..., N\},$$

$$\underbrace{\begin{bmatrix} u_i^j(t) \\ \vdots \\ u_i^j(t+k) \\ \vdots \\ u_i^j(t+N) \end{bmatrix}}_{\mathbf{u}_i^j(t)} \rightarrow \underbrace{\begin{bmatrix} u_i^j(t) \\ \vdots \\ u_i^j(t+k-1) \\ u_i^j(t+k+1) \\ \vdots \\ u_i^j(t+N) \end{bmatrix}}_{\mathbf{u'}_i^j(t)},$$

where $\mathbf{u}_i^j(t) \in \mathbb{R}^{N+1}$ and $\mathbf{u'}_i^j(t) \in \mathbb{R}^{N'+1}$, being

$$N' = N - \sum_{k=0}^{N} \left(1 - \delta_i^j(t+k)\right)$$

Note that this operation, i.e. to reduce the vector $\mathbf{u}_i^j(t)$ to $\mathbf{u'}_i^j(t)$, can be achieved by means of a simple change of variable:

$$\mathbf{u}_i^j(t) = M\mathbf{u'}_i^j(t),$$

where $M \in \mathbb{R}^{N+1} \times \mathbb{R}^{N'+1}$.

For example, if $N = 3$:

$$\mathbf{u}_i^j(t) = \begin{bmatrix} u_i^j(t) \\ u_i^j(t+1) \\ u_i^j(t+2) \\ u_i^j(t+3) \end{bmatrix},$$

and we are assuming these values: $\delta_i^j(t) = 1$, $\delta_i^j(t+1) = 1$, $\delta_i^j(t+2) = 0$ and $\delta_i^j(t+3) = 1$. That means that the dimension of $\mathbf{u}_i^j(t)$ has to be reduced in one order, so $N' = 2$ and

$$M = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 1 \end{bmatrix},$$

this matrix provides the reduced vector:

$$\mathbf{u'}_i^j(t) = \begin{bmatrix} u_i^j(t) \\ u_i^j(t+1) \\ u_i^j(t+3) \end{bmatrix}.$$

□

Therefore, $\mathbf{u'}_i^j(t)$ contains only the ordered items that are non-zero.

This optimization problem will be solved as many times as possible combinations with the values of $\{\delta_i^j(t), ..., \delta_i^j(t+N)\}$, to avoid this variable in the optimization, so we will obtain the same number of values of the objective function. The optimal combination of the values of $\{\delta_i^j(t), ..., \delta_i^j(t+N)\}$ corresponds with the one that provides the minimal value of the objective function.

It is necessary to pay special attention to the constraints while solving this problem. It is not possible to impose the whole matrix of constraints to the reduced vector $\mathbf{u'}_i^j(t)$, so it is necessary to also apply the change matrix M to the matrix of constraints to impose them only to the control components that we are considering.

C. CC-MPC

In this subsection, the way to treat the constraints stochasticastically is presented. In (10), the aggregate demand $d(t)$ has associated a stochastic disturbance, due to the uncertain nature of $d(t)$. As the state is influenced by additive uncertainties $d(t)$, the constraints can not be represented in a deterministic way. Therefore they are rewritten in a probabilistic manner, e.g.:

$$P(s(t+k) \geq s_{min}) \geq 1 - \delta_s, \quad \forall k \in \{1, .., N\},$$

where δ_s is the probability of failure, so it is the risk bound of stockout. Developing the last expression along the prediction horizon, and assuming that the disturbances behave as a function of a certain probability distribution, it is possible to calculate or estimate the mean and standard deviation of the state variable. For example, for the first instant of the prediction horizon and assuming that the perturbations behave as a normal distribution with mean μ and standard deviation σ, i.e., $d(t) = N(\mu, \sigma)$, we get:

$$P(s(t+0) + o(t+0) - d(t+0) \geq s_{min}) \geq 1 - \delta_s,$$

which can be normalized as follows:

$$P\left[\tfrac{s(t+1)-s(t+0)-o(t+0)-\mu}{\sigma} \geq \tfrac{s_{min}-s(t+0)-o(t+0)-\mu}{\sigma}\right] \geq 1 - \delta_s$$

$$P\left[\tfrac{s(t+1)-s(t+0)-o(t+0)-\mu}{\sigma} \leq \tfrac{s_{min}-s(t+0)-o(t+0)-\mu}{\sigma}\right] \leq \delta_s$$

$$\varphi\left(\frac{s_{min} - s(t+0) - o(t+0) - \mu}{\sigma}\right) \leq \delta_s$$

$$\frac{s_{min} - s(t+0) - o(t+0) - \mu}{\sigma} \leq \varphi^{-1}(\delta_s),$$

where $\varphi(\cdot)$ is the probability distribution function. This allows us to write a constraint of the form:

$$-o(t+0) \leq s(t+0) - s_{min} + \varphi^{-1}(\delta_s)\sigma + \mu.$$

Next, for the second time instant in the prediction horizon:

$$\begin{aligned} &P(s(t+2) \geq s_{min}) \geq 1 - \delta_s \\ &P(s(t+1) + o(t+1) - d(t+1) \geq s_{min}) \geq 1 - \delta_s \\ &P((s(t+0) + o(t+0) - d(t+0)) + o(t+1) \\ &-d(t+1) \geq s_{min}) \geq 1 - \delta_s \\ &P(s(t+0) + o(t+0) - d(t+0)) + o(t+1) \\ &-d(t+1) \geq s_{min}) \geq 1 - \delta_s. \end{aligned}$$

Following the same reasoning of the previous case, we have:

$$\varphi\left(\frac{s_{min} - s(t+0) - o(t+0) - o(t+1) - 2\mu}{\sigma\sqrt{2}}\right) \leq \delta_s$$

$$\frac{s_{min} - s(t+0) - o(t+0) - o(t+1) - 2\mu}{\sigma\sqrt{2}} \leq \varphi^{-1}\delta_s,$$

which allows us to write the following constraint:

$$\begin{aligned} &-o(t+0) - o(t+1) \leq \\ &s(t+0) - s_{min} + \varphi^{-1}\delta_s \cdot \sigma\sqrt{2} + 2\mu. \end{aligned}$$

In general, for a prediction horizon N, we have the following constraint that has to be included in the optimization problem behind the design of the MPC to implement the chance constraints:

$$-\begin{bmatrix} 1 & 0 & 0 & \cdots & 0 \\ 1 & 1 & 0 & \cdots & 0 \\ 1 & 1 & 1 & \cdots & 0 \\ \vdots & & & & \vdots \\ 1 & 1 & & \cdots & 1 \end{bmatrix} \begin{bmatrix} o(t+0) \\ o(t+1) \\ o(t+2) \\ \vdots \\ o(t+N-1) \end{bmatrix} \leq \begin{bmatrix} 1 \\ 1 \\ 1 \\ \vdots \\ 1 \end{bmatrix} s(t+0)$$
$$+ \begin{bmatrix} 1 & 1 & 1 \\ 1 & 2 & \sqrt{2} \\ 1 & 3 & \sqrt{3} \\ \vdots & \vdots & \vdots \\ 1 & N & \sqrt{N} \end{bmatrix} \begin{bmatrix} -s_{min} \\ \mu \\ \varphi^{-1}(\delta_s)\sigma \end{bmatrix}.$$

IV. Case Study and Results

In this section, we apply the proposed CC-MPC[2] to one of the most expensive drugs that is used in these hospitals. In addition, this drug deserves special attention since it must be stored in a fridge, which makes even more important to reduce its average stock level. The real name and price of the drug will not be presented in this paper due to confidentiality reasons.

Regarding the controller, a horizon of 8 days has been considered. The evolution of the stock is modeled using the discrete linear model (10). The orders of this drug have a minimum amount of 4 units and the maximum has been set to 1000. The price of the drug is 250 euros per unit and each order placed implies an additional cost of 2 euros. The deliveries of this drug usually have a delay of 2 days with respect to the moment in which the order was placed. Finally, the demand term of (10) is non deterministic. A probabilistic characterization of its behavior has been calculated for this drug based on historical data. As a result, we have modeled the daily demand as a normal random variable with $\mu = 20$ and standard deviation $\sigma = 15$.

For simplicity, neither storage cost nor storage limits have been considered at this stage of our work. The only implemented constraint with respect to the stock is that the probability of stockout event has to be lower than 0.001, i.e., we request a reliability level of 99.999 %. This choice for the reliability level is to prioritize the satisfaction of the clinic needs.

A 600 days simulation of the proposed approach is shown in Figure 2. In blue, the evolution of the stock using CC-MPC is shown. In red, the real evolution of the stock according to the hospital data is shown. In both cases, the stock was always positive, but in the case of CC-MPC the average level was 204 units with a standard deviation of 113, which outperforms the results registered by the hospital (a mean of 451 units and a standard deviation of 229). Note that, for the price considered, this difference corresponds to an amount of more than 60000 euros that is invested *frozen* unnecessarily. Finally, it is also interesting to notice that during the studied period the hospital placed 58 orders while

[2]The problem could be solved also using *Mixed Integer Techniques* but it would imply a much higher computational cost. One of the advantages of CC-MPC is that the computational cost is the same than the one for a classic MPC.

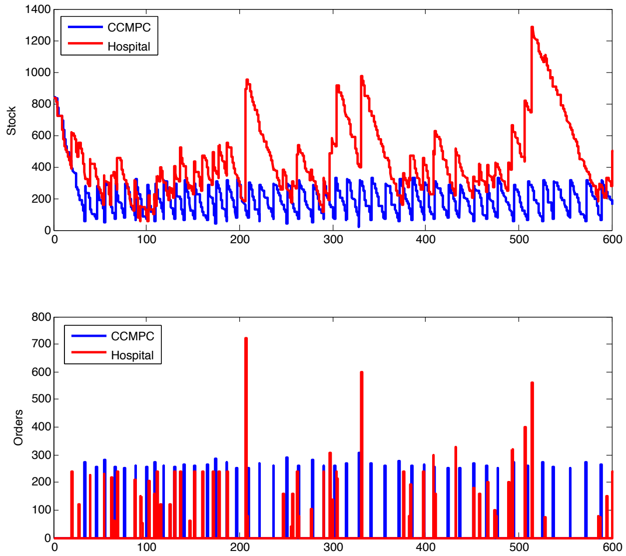

Fig. 2. Real and simulated stock evolution and placed orders.

the CC-MPC placed 44. That is, the CC-MPC obtained better results even with less orders.

The optimization has to be made taking into account the constraints given by (5)-(8). A problem is solved at every sampling time to compute a control sequence u that takes the system to the desired reference. For this drug, the stock reference (security stock) has been set to 2.

A word of caution has to be said regarding the results at this point: there may be some uncertainty associated with the real data. Sometimes either the drug dispensations or the arrivals of new items are recorded later than they occurred. Another interesting issue regarding the real evolution is its big peaks, which are usually associated to orders placed before holiday periods (no orders can be placed then). In any case, the difference between the reality and the simulation is big enough to believe that the application of this kind of policies in this context is promising.

All optimization problems, solved for the exhaustive algorithm, were computed using a linear programming (*linprog* in *Matlab*), on a machine with an Intel Core 2 Duo CPU with 3.33 GHz and 8 GB RAM.

V. Conclusions

In this paper we have described a control-based methodology for decision-making in a pharmacy department to address prevention and control problems in the inventory management. As it can be seen, inventory management is one of the main tasks that a pharmacy department has to carry out in a hospital. It is a complex problem that requires to establish a tradeoff between different and contradictory optimization criteria.

The proposed methodology optimizes the management of the stock while guaranteeing with a very high probability that the drugs will be available for the patients. In this sense, the MPC framework is particularly useful because of its favorable properties, such as ease of constraint-handling.

Finally, it is worthwhile to mention that the proposed technique may provide important economical savings based on the reduction of the average level of stocked drugs while still guaranteeing the satisfaction of the clinical needs of the hospital. Future work will include the extension of the current framework to consider some of the issues that have not been addressed in this paper, like perturbations or time delays, and the real implementation of this control policy into the hospitals that collaborate in this project. It will be interesting also to compare this results with a worst case approach and others probability levels. Finally, a more detailed model of the demand can be developed too.

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Capítulo 12

RESULTADOS Y DISCUSIÓN

El trabajo desarrollado enlaza con los objetivos del estudio.

En primer lugar, se han estudiado nuevas técnicas de estimación de la demanda sin realizar ningún tipo de hipótesis simplificadoras sobre su distribución, sino directamente en base a datos históricos. Concretamente, en el trabajo desarrollado para el congreso Emerging Technology and Factory Automation 2014, titulado "Optimizacion of the demand estimation in hospital pharmacy" se han analizado y comparado diferentes métodos de estimación de la demanda, además del método habitual usado por los hospitales.

Se presentan diferentes técnicas:

- Las series temporales son modelos de predicción basados en datos históricos de una variable que son analizados para descubrir patrones como tendencias, ciclos o estacionalidad, que son proyectados hacia el futuro. Estas técnicas son útiles para predecir a medio y corto plazo [18].
  - Enfoque simple (simple approach): se asume que el valor de la variable no cambia de un periodo a otro y que el proceso cambia muy lentamente. Además es un método impreciso, no considera variaciones por estaciones o ciclos y sobreestima las variaciones aleatorias. Sin embargo es la técnica con la mejor tasa coste-eficiencia [26]. Es recomendable como punto de partida hacia otros métodos más sofisticados.
  - Promedio móvil simple: es la media del periodo de tiempo más corto. Este método utiliza los datos más relevantes de los últimos n periodos y la actualización entre periodos, eliminando la primera observación y agregando la última. Otra ventaja es que los cálculos son muy simples y el sistema es flexible, considerando que la tendencia no se ajusta a una función matemática particular. La media móvil depende de n, si el valor de n es grande la media móvil responderá lentamente a cambios y si es pequeño la respuesta es más rápida (Pérez 2007).
  - Suavizado o alisado exponencial: la idea básica de esta técnica es predecir partiendo de la media, la demanda más reciente y una constante de suavizado o alisado que permite disminuir la influencia de valores muy distantes. Si la constante tiene un valor grande tienen más peso

los valores recientes mientras que un valor pequeño de la constante le da más peso a los cambios sustanciales en el comportamiento de la variable en estudio, de manera que el modelo responde más rápidamente a cambios en la demanda. Este método es recomendable cuando el horizonte temporal de predicción es corto, cuando se desconocen factores independientes que afecten a la demanda y cuando sea deseable que la predicción siga la tendencia y la estacionalidad (Pérez 2007).

  - Box-Jenkins (ARIMA): este modelo integra un modelo autorregresivo integrado con la media móvil. Es más sofisticado que los anteriores.

- Los modelos causales asumen una relación causa-efecto entre una variable dependiente (demanda) y otras independientes (Pérez 2007). Pueden aplicar una regresión lineal simple o múltiple. Lo más importante es que pueden ser usados para predecir puntos cambiantes en la demanda. En cambio, las series temporales predicen el patrón de la demanda, pero no predicen picos en los niveles de la misma. De ahí que los modelos causales sean generalmente más exactos que las series temporales para formular predicciones a medio y largo plazo.

Estos métodos de predicción de la demanda se han aplicado en un conjunto de 10 medicamentos, todos ellos de dispensación a pacientes externos, seleccionados por su alto valor económico. Todas las técnicas se han aplicado en los 10 medicamentos diferentes. Para el análisis se han utilizado los datos históricos recogidos de salidas y entradas en un hospital durante un periodo de 20 meses (de enero de 2012 a agosto de 2013) y la estimación se ha realizado a 28 semanas. Los resultados se comparan también con el método habitual utilizado por el hospital, que basa la estimación en la media del consumo de los últimos 12 meses.

Ninguno de los métodos estudiados resultó ser el más óptimo en todos los casos. El método tradicional basado en los consumos de los 12 meses proporciona la mejor estimación en 5 de los 10 medicamentos estudiados tras un análisis de la media y la desviación típica del error de estimación. El hecho de que este método haya obtenido los mejores resultados puede deberse también a que el histórico de datos usado es mayor que el utilizado para los otros métodos (52 semanas). El promedio móvil simple, el alisamiento exponencial y el método ARIMA proporcionan la mejor estimación para un fármaco concreto cada uno. El modelo causal, concretamente la regresión lineal simple, es el más óptimo para otros 2 fármacos.

Los resultados reflejan, por tanto, que la utilización del mismo método para todos los medicamentos no es adecuada, concluyéndose de aquí que debe establecerse un método de estimación de demanda individualizado para cada medicamento. Esta mejora en la estimación de la demanda ha permitido a continuación estudiar nuevas técnicas de optimización de stock.

A continuación se han evaluado y comparado 3 técnicas de gestión diferentes basadas en MPC con el objetivo de optimizar el número de pedidos que realiza un Servicio de Farmacia Hospitalaria en trabajo publicado en el congreso Emerging Technology and Factory Automation 2014, titulado "Application of robust model predictive control to inventory management in hospitalary pharmacy". Estas técnicas evaluadas se fundamentan en la utilización de un modelo matemático para predecir la evolución de stock a partir de las estimaciones disponibles acerca del comportamiento esperado de la demanda. Se trata de:

- Gestión con restricciones probabilísticas (GRP), donde se consideran la media y la desviación estándar de los datos históricos de la demanda para garantizar la satisfacción de las restricciones impuestas por el Servicio de Farmacia (por ejemplo, existencias superiores al stock de seguridad) con una cierta probabilidad.

- Gestión basada en múltiples escenarios (GME), en la que las decisiones de adquisición de medicamentos se toman de forma que garantice la satisfacción de las restricciones del Servicio de Farmacia en escenarios de evolución de la demanda basados en datos históricos. Es decir, si la demanda sigue patrones de comportamiento similares a los ya registrados, las restricciones son satisfechas.

- Gestión basada en árboles de evolución (GAE), que es una variación del método anterior que agrupa los escenarios más probables en un árbol de posibilidades que se va ramificando a la vez que el comportamiento de los escenarios de evolución de la demanda diverge significativamente.

Estas técnicas se han evaluado en simulación para la gestión de un medicamento termolábil de alto impacto económico. Una simulación de 230 días ha permitido comparar la evolución esperada del stock siguiendo la política del hospital con la que se obtendría utilizando las alternativas consideradas. En concreto, el hospital ha realizado en dicho periodo 26 pedidos para obtener 394 unidades almacenadas de media y 186 de desviación típica. Frente a ello, los resultados de las técnicas evaluadas fueron: GRP (13 pedidos, 291 unidades de media y desviación estándar de 101), GME (18, 245 y 92) y GAE (13, 183 y 89). La diferencia entre el caso real y la simulación es lo suficientemente grande tanto en número de pedidos realizados como en el promedio almacenado como para considerar útil y ventajosa a todos los niveles la aplicación de este tipo de políticas en este contexto. Concretamente, teniendo en cuenta que el coste del medicamento es de 250 euros, el ahorro estimado podría ser como mínimo de 25000 euros. Se ha estudiado también la minimización del riesgo de rotura de stock mediante diferentes métodos en "Análisis y minimización del riesgo de rotura de stock aplicado a la gestión en farmacia hospitalaria" (Farmacia Hospitalaria 2011) y en "Control predictivo aplicado a la gestión de stocks en farmacia hospitalaria: un enfoque orientado a la minimización del riesgo" (Revista Iberoamericana de Automática e Informática industrial 2013).

En "Análisis y minimización del riesgo de rotura de stock aplicado a la gestión en farmacia hospitalaria" (Farmacia Hospitalaria 2011) se determina el valor que debería tomarse como stock de seguridad en un medicamento concreto estudiado y seleccionado por su alto coste y por la inmediatez de su necesidad en la actividad diaria de un hospital real. Este stock de seguridad se establece en función del nivel de riesgo y del número de días que se desee resistir sin rotura de stock. Adicionalmente se calcula también el valor que debería tomar dicho stock conforme a diferentes reglas utilizadas por los Servicios de Farmacia y se comparan con el método propuesto.

En "Control predictivo aplicado a la gestión de stocks en Farmacia Hospitalaria: un enfoque orientado a la minimización del riesgo" (Revista Iberoamericana de Automática e Informática industrial 2013) se aplica el MPC en simulación con datos reales de un hospital desde una perspectiva de minimización del riesgo.

Se añaden acciones de mitigación con el objetivo de reducir el impacto de los posibles riesgos que pueden ocurrir. Por lo tanto, se añaden al problema inicial nuevas variables de decisión. En la comunicación para el congreso Conference on Decision and Control 2014, titulada "An application of chance-constrained model predictive control to inventory management in hospitalary pharmacy" se aplica MPC integrado con restricciones probabilísticas a un medicamento termolábil de alto coste.

Se ha establecido un mínimo de 4 unidades y un máximo de 1000. El precio es de 250 euros por unidad. Cada pedido tiene un coste adicional de 2 euros y la entrega se realiza en 2 días. Se ha realizado una simulación de 600 días y se ha comparado con la evolución del stock siguiendo la técnica utilizada por el hospital.

El stock medio obtenido con la nueva técnica es de 204 unidades con una desviación estándar de 113. Con el método del hospital al resultado es de 451 unidades de media y una desviación estándar de 229. El ahorro estimado por la reducción del stock almacenado es de más de 60000 euros. Además, el hospital realiza 58 pedidos mientras que con esta técnica el número de pedidos se reduce a 44. Asimismo se ha estudiado la aplicación de restricciones probabilísticas para los problemas de gestión en este contexto en "Stock management in hospital pharmacy using chance-constrained model predictive control" (Computers in Biology and Medicine 2016). Es una extensión de dos trabajos previos (CDC 2014 y ETFA 2014) en los que se asume un comportamiento Gaussiano de la demanda. En este trabajo el controlador puede ser aplicado incluso si la demanda sólo está caracterizada estadísticamente basándose en datos históricos.

En el caso particular de problemas de control estocásticos, cuya evolución en el tiempo es aleatoria como el caso que nos ocupa, donde el sistema que se controla es objeto de incertidumbres, la política de control puede hacer frente al peor escenario posible y garantizar que las variables cumplan las restricciones a costa de aplicar una política más conservadora. Con el fin de suavizar esa robustez es aceptable asumir un nivel de riesgo más bajo formulando las restricciones del problema de una forma probabilística. Para ello se pueden implementar restricciones probabilísticas en combinación con el MPC, que ha sido la técnica aplicada en este trabajo. Se define un modelo matemático para el sistema cuyo objetivo es satisfacer la demanda, reducir el stock y minimizar el número de pedidos para adecuar la carga de trabajo al personal. Para satisfacer la demanda debe reducirse la probabilidad de rotura de stock. La demanda es desconocida de antemano y la entrega también puede ser un factor de incertidumbre. Para ello se establece un stock de seguridad: con un valor mínimo fijo y un máximo variable. El máximo almacenable también debe considerarse puesto que el espacio es limitado. Se tendrá en cuenta también el coste global del pedido (debe llegar a un importe mínimo para que el proveedor lo sirva) y el número de artículos pedidos en cada solicitud. Asimismo se consideran los días festivos y fines de semana en los que no se van a realizar pedidos y tampoco se van a efectuar entregas. Y, por último, el valor de los medicamentos solicitados, ya que el presupuesto supone también una restricción.

Se aplica esta técnica en simulación a dos medicamentos termolábiles. Se ha establecido un mínimo de 4 unidades y un máximo de 1000. El precio es de 227 y 298 euros por unidad respectivamente. Cada pedido tiene un coste adicional de 2 euros y la entrega se realiza en 2 días. Los valores de stock iniciales son 500 y 1520 respectivamente. En los 360 días del periodo de estudio el hospital realizó 9 pedidos de uno de los medicamentos y 25 del otro. El resultado, aplicando la estrategia en estudio, hubiese sido de 5 y 15 pedidos respectivamente. Asimismo, el stock medio hubiese sido de 39 unidades de uno de los medicamentos y 770 unidades del otro, 4 unidades menos del primero y 91 menos del segundo que siguiendo la metodología del hospital.

Por otra parte, dado que se realizarían menos pedidos, la desviación estándar y las fluctuaciones son algo mayores con la simulación. No se ha producido ninguna rotura de stock. Esta mejora de la gestión con las nuevas técnicas aplicadas se traducirían en un ahorro económico de 1000 euros de media con el primer medicamento y de 27118 euros con el segundo. En conjunto se hubieses realizado un 40

Los resultados finales de la simulación es que se reduce el stock medio y la carga de trabajo mientras que se satisface la demanda al 100

Por último se ha desarrollado un nuevo sistema de soporte a la decisión del farmacéutico basado en técnicas de control predictivo, que ha sido validado en un entorno real mediante dos pruebas piloto llevada a cabo con un conjunto de medicamentos de un mismo laboratorio.

En “An application of economic model predictive control to inventory management in hospitals” (Control Engineering Practice 2018) se realiza la primera validación de la técnica en un hospital durante un periodo de 4 meses. Se han seleccionado 10 medicamentos de un mismo proveedor para el estudio. Con los datos de stock diarios de los medicamentos seleccionados para el estudio, el modelo matemático ha estimado cada día si pedir o no y cuánto pedir, teniendo en cuenta el histórico de datos de los 12 meses anteriores de consumos (salidas por unidosis, por dispensaciones urgentes y por pedidos de reposición, y entradas por recepciones de pedidos y devoluciones) y, por tanto, considerando múltiples escenarios extraídos de los mismos, incluidos casos extremos de consumos. Se han tenido en cuenta además una serie de restricciones que se han introducido en la ecuación como son el embalaje, pedido mínimo al proveedor, tiempo de entrega (se ha asumido un tiempo de entrega constante), stock máximo almacenable, stock mínimo necesario, precio de compra y máximo número de pedidos asumibles por el personal.

Esta metodología simula la evolución esperada de los niveles de stock durante un intervalo de tiempo, calculando el pedido óptimo para el conjunto de medicamentos considerado y automatizando así la gestión. El sistema trata de reducir al máximo la cantidad almacenada y el número de pedidos pero garantizando la satisfacción de la demanda en un cierto periodo de tiempo en el peor escenario que pudiera darse según los datos de consumos reales de los últimos 12 meses.

En último caso, el farmacéutico puede, si no se siente cómodo con la sugerencia del sistema (vacaciones, cierres de laboratorio, aumento de demanda prevista, oferta temporal...cualquier factor externo que pueda afectar a la demanda o la entrega), forzar un pedido. Sin embargo se han seguido fielmente las recomendaciones del sistema en todo el periodo de estudio.

Se han medido los siguientes parámetros:

- el stock medio que es indicativo del dinero inmovilizado
- el stock máximo y el stock mínimo alcanzados en el periodo en estudio

- roturas de stock
- la desviación estándar que informa de las fluctuaciones del stock
- tasa de pedidos: número de días en los que se ha realizado pedido frente al número de días total del estudio. Este parámetro se relaciona directamente con la actividad generada en el Servicio de Farmacia.
- Número medio de artículos pedidos cuando éstos se han formalizado

Comparando con el mismo periodo del año anterior al estudio se ha reducido considerablemente tanto el stock máximo almacenado, como el stock promedio. Se ha liberado un total de 579 unidades, que se traduce en un ahorro económico estimado de 644.89 euros. Esta metodología agrupa los medicamentos para efectuar los pedidos, de ahí que se haya producido también una amplia reducción en su número. Se han realizado pedidos un 12.5 % de los días frente al 31 % en el mismo periodo del año anterior. En consecuencia la carga de trabajo del Servicio de Farmacia también se ve disminuida.

No se ha producido ninguna rotura de stock, aunque para 2 medicamentos el stock ha sido de cero en ciertos momentos.

En contraste con los trabajos publicados anteriormente, donde se han llevado a cabo simulaciones para evaluar distintos métodos estocásticos de MPC al control de los niveles de stock de medicamentos individuales como un problema simple (por ejemplo, no se han considerado ni límites ni costes de almacenamiento), este trabajo se ha desarrollado con un grupo de medicamentos que pertenecen todos al mismo proveedor, lo cual es más práctico en un escenario real.

Al mismo tiempo, con idea de que el personal del Servicio de Farmacia adopte fácilmente el método y lo introduzca en su dinámica, la estrategia se ha diseñado como un sistema de apoyo a la decisión del farmacéutico.

Pese a estas aportaciones y a los buenos resultados obtenidos, esta metodología también presenta sus inconvenientes. En primer lugar, es necesario disponer de un stock actualizado siempre para que los datos introducidos en el sistema sean reales y pueda estimar y predecir con exactitud de acuerdo al stock real. Esto a veces no ocurre por motivos de acúmulo de trabajo, o bien no se ha cursado la salida del medicamento o no se ha recepcionado informáticamente un pedido ya recibido por falta de tiempo.

Por otra parte, en distintos momentos del estudio el personal del Servicio de Farmacia no se ha sentido cómodo con el nivel de riesgo asumido por el sistema, excesivo según su percepción por la costumbre de disponer de mayor stock. De hecho, en una ocasión se forzó un pedido. Es necesario ajustar ese nivel de riesgo y generar más confianza en el personal.

Sería interesante ampliar este estudio explorando nuevas formas de implementarlo en el día a día de un Servicio de Farmacia, mejorando su utilidad y las limitaciones mostradas.

En “A data-based model predictive decisión support system for inventory management in hospitals” (Journal of Biomedical and Health informatics 2020) se lleva a cabo una segunda validación en el mismo hospital con los mismos medicamentos durante un periodo de 4 meses, con más restricciones añadidas al diseño del sistema y teniendo en cuenta el histórico de datos de los 24 meses anteriores, éste ha calculado diariamente la cantidad a pedir de cada uno de ellos para cubrir periodos de 2 a 8 días, el importe total del pedido y la probabilidad de rotura de stock durante ese mismo periodo de 8 días en caso de no formalizar el pedido. El motivo de establecer un periodo mínimo de 2 días es que 2 días es el tiempo de entrega del proveedor.

Este procedimiento ha permitido al personal del Servicio de Farmacia valorar todas estas propuestas cada día y tomar la decisión última de pedir o no y del número de días a cubrir en función del riesgo de rotura de stock dispuesto a asumir. Es decir, que se trata de una herramienta de soporte para la toma de decisión de pedir o no, sin embargo, se han seguido fielmente las recomendaciones en cuanto a las cantidades.

Se han medido los mismos parámetros que en el estudio anterior:

- el stock medio que es indicativo del dinero inmovilizado
- el stock máximo y el stock mínimo alcanzados en el periodo en estudio
- roturas de stock
- la desviación estándar que informa de las fluctuaciones del stock

- tasa de pedidos: número de días en los que se ha realizado pedido frente al número de días total del estudio. Este parámetro se relaciona directamente con la actividad generada en el Servicio de Farmacia.
- Número medio de artículos pedidos cuando éstos se han formalizado

Comparando los resultados con los que se hubiesen obtenido en caso de aplicar MPC puro como en el trabajo anterior, se deduce que el stock medio se hubiese reducido más, ahorrando un total de 649.5 euros, reduciéndose también el número de pedidos a 31, frente a los 34 realizados en el periodo de la prueba. Sin embargo, la mejora del último método se traduce principalmente en la cobertura de la demanda: no se ha producido ninguna rotura de stock, mientras que aplicando MPC puro se hubiesen producido 4, debido fundamentalmente a diferencias entre la demanda real y la media considerada para las predicciones.

Si comparamos con los 4 meses anteriores al periodo de estudio, se concluye que con las nuevas técnicas se reduce el stock medio y se reducen los picos alcanzados o se mantienen más cerca de la media. El número de pedidos también se reduce un 19 %, de 42 a 34. Sin embargo, la media del valor inmovilizado aumenta en 366.73 euros debido al leve incremento de los niveles de stock de algunos de los medicamentos más caros. Posiblemente esto se deba a picos en los históricos de la demanda, de manera que este stock extra ayudaría a minimizar los riesgos de rotura de stock y, por consiguiente, satisfaría la pasada demanda real. Los menores valores de stock de estos fármacos más caros se alcanzan con la política de MPC puro.

En este trabajo se ha utilizado una estrategia estocástica de MPC diferente denominada MPC basado en múltiples escenarios, que parte de los datos históricos de acciones del propio Servicio de Farmacia para predecir la evolución del stock en un hospital real. Ésta es la principal diferencia con respecto a los trabajos anteriores: se basa en los datos históricos de acciones y aprende de los nuevos datos aportados al sistema cada día. Otra novedad es que el farmacéutico es el que decide entre las posibilidades presentadas por el controlador, que aplica MPC basado en datos para diferentes horizontes y niveles de riesgo. El sistema es utilizado como referencia puesto que a la hora de ejecutar un pedido hay múltiples factores a considerar que no pueden ser implementados en el controlador, como periodos vacacionales, festivos, cierres de laboratorios, fluctuaciones concretas de la demanda, etc. De esta manera a las ventajas que aporta el sistema con técnicas de MPC basado en múltiples escenarios, se añade la experiencia y criterio del farmacéutico.

Los resultados obtenidos tras un periodo de prueba de 4 meses se comparan con el controlador basado en MPC implementado en el Servicio de Farmacia en el estudio anterior que se basa en pronóstico MPC puro. La comparación se complementa con los resultados de la política habitual seguida por el hospital, es decir, la técnica del punto de pedido.

En ambos casos las técnicas propuestas de optimización del stock han demostrado mejorar la gestión con respecto a la metodología habitual, garantizando el abastecimiento de la demanda en todo momento, y proporcionando además importantes ventajas como la disminución del espacio de almacenamiento necesario, reducción de la carga de trabajo mediante la reducción del número de pedidos, además de ahorros económicos en base a la disminución del nivel medio de stock y mayor control del stock (disminuye la desviación típica del nivel de stock, manteniéndose éste con menos fluctuaciones en el tiempo) y del nivel de riesgo asumido. A lo largo de todo el proyecto se han implementado, por tanto dos tipos de métodos: técnicas de control predictivo directamente y técnicas de control basado en datos.

Capítulo 13

CONCLUSIONES

La gestión de stocks es una tarea relevante en un centro hospitalario y su optimización repercutirá, por tanto, en el funcionamiento global del hospital. Se trata de un problema complejo que requiere establecer un equilibrio entre criterios que resultan contradictorios como pueden ser la disponibilidad de medicamentos y el coste o el espacio de almacenamiento. En este proyecto se han aplicado técnicas avanzadas de estimación y control orientadas a esta particular problemática de la gestión de stocks y ha resultado ser prometedora y fácil de implementar.

13.1. Estimación de la demanda

En primer lugar, se han estudiado diferentes métodos de estimación de la demanda con objeto de disminuir su incertidumbre y con ello el stock almacenado y el dinero inmovilizado. Ninguno de los métodos evaluados ha resultado ser el más óptimo en todos los casos, por lo que se puede concluir que no es adecuado utilizar un único método para todos los medicamentos y que debe establecerse de forma individualizada para cada uno.

13.2. Aplicación de técnicas de MPC en simulación

Esta mejora en la estimación de la demanda ha permitido a continuación aplicarla en simulación al estudio de diferentes técnicas de gestión basadas en MPC. Estas técnicas parten de datos históricos de consumos, pedidos, roturas de stock, etc. para predecir la evolución esperada de los niveles de stock y con ello optimizar la política de gestión. Los resultados de las distintas simulaciones realizadas con diferentes medicamentos y técnicas demuestran la optimización de la gestión a todos los niveles garantizando el abastecimiento y proporcionando importantes beneficios como la disminución del volumen inventariado, con la consiguiente liberación de espacio y reducción del dinero inmovilizado.

13.3. Validación en entorno real

Por último se ha diseñado un sistema que ayuda a la toma de decisión de qué, cuánto y cuándo pedir y, por tanto, automatiza en gran medida la ejecución de pedidos. Este sistema de soporte al farmacéutico se ha validado en un entorno real mediante dos pruebas piloto desarrolladas en un hospital con un conjunto de medicamentos previamente seleccionados pertenecientes al mismo proveedor.

13.3.1. Primera prueba

En la primera prueba el sistema diseñado calcula el pedido óptimo para ese conjunto de medicamentos de manera que garantice la cobertura de la demanda con cierto grado de certeza (nivel de riesgo controlado) y cumpla el condicionante del importe mínimo establecido por el laboratorio. Este método, a diferencia de los trabajos anteriores, es más práctico y se acerca más a la actividad real de un Servicio de Farmacia al trabajar por proveedor y no por medicamento.

Siguiendo con total fidelidad las recomendaciones del sistema, el resultado obtenido fue satisfactorio en términos de roturas de stock (ninguna), reducción de los niveles medios y máximos de stock y disminución del número de pedidos en comparación con el mismo periodo del año anterior al estudio. Ésto puede traducirse además en ventajas a nivel económico (ahorro significativo por la reducción de stock) y de carga de trabajo por la minimización de pedidos.

A pesar de los beneficios obtenidos, esta metodología presenta también algunas limitaciones:

- Es importante ajustar el nivel de riesgo asumido por el sistema a la comodidad y confianza del farmacéutico. Un nivel de riesgo de rotura de stock elevado implica minimizar excesivamente los pedidos y genera cierta tensión y desconfianza en el personal.
- Hay factores que no se pueden introducir en una ecuación y que el sistema, por tanto, no puede controlar, como son vacaciones, festivos, cierres de laboratorios por inventario o actualización en sus sistemas, necesidades especiales previstas, descuentos por volumen de compra, etc. y que obligan a considerar solicitar mayores cantidades y a no respetar las recomendaciones del sistema.

13.3.2. Segunda prueba

En la segunda validación llevada a cabo en el mismo hospital y con los mismos medicamentos se introducen ciertas mejoras en el diseño del sistema, paliando las limitaciones comentadas.

El nuevo método permite al farmacéutico decidir si pedir o no y cuánto pedir en función del riesgo que esté dispuesto a asumir. El sistema ofrece una información detallada del riesgo de rotura de stock en los 8 siguientes días y recomienda la cantidad a pedir de cada medicamento en cada caso, siendo finalmente el personal el que, valorando esta información, toma la decisión última.

Esta metodología confiere autonomía al personal y se convierte así en una importante herramienta de soporte y ayuda para la toma de decisión que rodea a los pedidos, aportando mayor confianza al permitir controlar la casuística que es imposible codificar en una ecuación y que hace imprescindible el factor humano en este sentido.

Los resultados en este caso fueron igualmente satisfactorios en cuanto a número de pedidos, niveles de stock y desabastecimientos, aplicándose una estrategia mejorada con respecto a la anterior (MPC basado en múltiples escenarios).

13.4. Aportaciones

13.4.1. Mejoras en aspectos generales

La aplicación de este tipo de técnicas aporta ventajas a todos los niveles: reducción de stock, liberación de espacio, ahorro económico, optimización de pedidos y mejor aprovechamiento de los recursos humanos.

13.4.2. Optimización del pedido

Estos métodos permiten trabajar a nivel de proveedor y no sólo de medicamento, de manera que son capaces de optimizar el pedido teniendo en cuenta la totalidad de medicamentos que pueden solicitarse al mismo laboratorio, siendo éste uno de los elementos clave en la reducción de la tasa de pedido y como resultado, de la carga de trabajo. Además de evitar excedentes de medicamentos que únicamente se solicitan a veces para alcanzar un determinado importe mínimo de pedido.

13.4.3. Confianza

A diferencia de la política clásica de gestión, la gran ventaja que aporta concretamente el último método evaluado, además de la optimización de la gestión comentada, es la confianza y seguridad que proporciona al personal. Esta metodología ha demostrado ser una herramienta muy útil y fácilmente aplicable de ayuda a la toma de decisiones de cuánto y cuándo pedir, conociendo de antemano y explícitamente el nivel de riesgo asumido. El hecho de contar con los datos de probabilidad de rotura de stock y con la autonomía de decisión de si pedir o no y de cuántos días pedir, y no estar limitado a una cantidad ya establecida, confiere mayor confianza. Proporciona mucha información útil que permite al farmacéutico tomar mejores decisiones y no modifica la dinámica del Servicio de Farmacia.

13.4.4. Aplicabilidad

Es un sistema de fácil adopción e integración en el día a día. Podría considerarse un soporte de gran valor y una herramienta perfectamente aplicable a un Servicio de Farmacia en el que la gestión suele estar rodeada en el día a día de un alto grado de incertidumbre. Tratándose de un entorno hospitalario es de vital importancia que se cubra la demanda satisfactoriamente y cualquier soporte en este sentido que lo garantice es de gran ayuda y utilidad.

13.5. Limitaciones

13.5.1. Diseño

Por seguridad, el desarrollo del sistema fue independiente del programa de gestión del centro. Por lo tanto, obliga a introducir manualmente los datos de stock cada día de cada medicamento.

13.5.2. Stock actualizado

Otra limitación de esta metodología es que precisa disponer de un stock actualizado para que las estimaciones sean válidas y acordes a las existencias reales. Esta condición no siempre se cumple, sobre todo en determinados momentos de sobrecarga de trabajo.

13.6. Investigaciones futuras

13.6.1. Ampliación

Como posibles líneas futuras de investigación, se podría ampliar a otros medicamentos e incorporar otros proveedores al sistema. Sin embargo, el diseño actual supone una limitación para ampliar a mayor número de artículos por el hecho de tener que introducir manualmente los datos de stock cada de cada uno. Es factible de abordar con 10 artículos como en las pruebas realizadas, pero resultaría demasiado tedioso con un número mayor.

Como mejora, por tanto, podría considerarse la conexión directa del sistema con la base de datos del hospital, de forma que tomase directamente estos datos. De esta manera sí sería realmente útil y práctico implementar este procedimiento y utilizarlo de forma generalizada con todos los medicamentos y proveedores.

13.6.2. Cooperación con otros centros

Sería interesante colaborar con otros centros que compartan el mismo sistema informático de gestión de manera que se puedan explotar datos de medicamentos comunes. Esto permitiría en un momento dado optimizar aún más la gestión permitiendo una rotación de artículos entre centros, por ejemplo de aquellos próximos a caducar en un hospital que puedan tener salida en otro, y facilitando también préstamos entre ellos que eviten roturas de stock. Se podría dar incluso un paso más creando una plataforma de compras común que realizara los pedidos a nivel centralizado aprovechando las sinergias entre centros y teniendo en cuenta la actividad concreta de cada uno, previo acuerdo con cada proveedor de la distribución de mercancía a cada hospital.

En las circunstancias de pandemia actuales, esta posibilidad de colaboración hubiese permitido analizar las tendencias de tratamiento utilizadas en otros centros y compartirlas, además de anticipar la adquisición de dichos medicamentos, escalonando los pedidos y evitando desabastecimientos por parte de los proveedores por la excesiva demanda.

En nuestro caso, por ejemplo, antes de que empezaran a llegar los primeros pacientes de Covid19, cuando aún reinaba el escepticismo, únicamente se hizo acopio de desinfectantes como el alcohol. Fue con la llegada de los primeros pacientes cuando se comenzaron a adquirir aquellos medicamentos que nos iban solicitando pero ya empezaban a escasear. Ante la creciente y desbordada demanda y, con el objetivo de llegar a todos los pacientes posibles, la AEMPS tomó el control de sus distribuciones, estableciendo criterios de uso, cambiando la disponibilidad de las distintas presentaciones, reduciendo el número de dosis o bien los días de tratamiento y, por último, dejando de servir para indicaciones no reflejadas en ficha técnica. Por otro lado, a medida que la pandemia se iba extendiendo empezaron a escasear también todos aquellos medicamentos habituales propios de pacientes intubados de UCI (midazolam, cisatracurio, propofol, fentanilo, dexmedetomidina, etc.). Comenzaron a demorarse los pedidos y a faltar stock en determinados proveedores, obligando a buscar alternativas, a solicitar préstamos a otros hospitales y a modificar los pedidos de uno a otro laboratorio en función de la disponibilidad. Finalmente ante el caos ocasionado por dicha situación desde el Servicio Andaluz de Salud (SAS) se decide que solamente se gestionen pedidos desde los hospitales de referencia de cada Provincia, en cantidades establecidas según el porcentaje de pacientes de UCI en cada una de ellas y, que desde cada centro de referencia (en nuestro caso Reina Sofía) se suministrase al resto de hospitales comarcales y privados de la Provincia en calidad de préstamo y según las asignaciones establecidas por los Servicios Centrales del SAS.

De la misma manera en la que se actuó en esta situación de crisis, se podría establecer una colaboración a nivel de gestión entre distintos centros que facilitase la adquisición centralizada y la distribución compartida entre hospitales facilitando la disponibilidad de medicamentos a todos los pacientes y evitando excedentes y acúmulos innecesarios.

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