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Spanish adaptation of the *Start Smart-Then Focus* tool for optimizing the use of antimicrobials

Adaptación nacional de la herramienta *Start Smart-Then Focus* para la optimización del uso de antimicrobianos

María Victoria Gil-Navarro[1], José María Gutiérrez-Urbón[2], Nabil El Fahimi[3], José Miguel Cisneros-Herreros[4]

[1]Unidad Clínica de Farmacia, Instituto de Biomedicina de Sevilla (IBIS)/Hospital Universitario Virgen del Rocío, Sevilla. Spain. [2]Servicio de Farmacia, Complejo Hospitalario Universitario La Coruña, La Coruña. Spain. [3]Servicio de Farmacia, United Lincolnshire Hospitals NHS Trust, United Kingdom. [4]Unidad Clínica de Enfermedades infecciosas, Microbiología y Medicina Preventiva, Instituto de Biomedicina de Sevilla (IBIS)/Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Sevilla. Spain.

Author of correspondence
María Victoria Gil-Navarro
Hospital Universitario Virgen del Rocío
Hospital General. Servicio de Farmacia. Semisótano
Avda. Manuel Siurot s/n.
41013 Sevilla, Spain.
Email:
mariav.gil.sspa@juntadeandalucia.es

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Abstract

Objective: The *Start Smart-Then Focus* tool of the United Kingdom's National Health System is a tool to be implemented in antimicrobial stewardship programs. The objective of this work is the adaptation of *Start Smart-Then Focus* tool to the Spanish health system.
Method: Delphi methodology was used. Two rounds were conducted by email. In the first, a questionnaire was sent out that included the criteria of the tool. These criteria were independently assessed by 16 experts. They rated the suitability and applicability of each criterion on a scale from 1 to 9 and made free comments on each one. The tool was modified and sent out again to all the experts. They re-scored the questionnaire individually, while aware of the anonymized results of the first round.
Results: The first questionnaire was made up of 19 indicators. Of these, 16 indicators had a median of more than 7 in suitability and applicability. However, regarding applicability, 3 indicators had a median of less than 7 and 10 had a minimum of less than 5. From the initial 19 indicators, we obtained 8 final indicators and 8 options were added to the sixth indicator.
Conclusions: It would be very useful to implement the Spanish adaptation of the *Start Smart-Then Focus* tool in antimicrobial stewardship programs at a national level. It would also contribute to improving the use of antimicrobials.

KEYWORDS
Antimicrobial stewardship; Anti-infective agents; Drug resistance; Drug utilization; Quality indicators, health care.

Resumen

Objetivo: La herramienta *Start Smart-Then Focus* del Sistema Nacional de Salud de Reino Unido es una herramienta de ayuda de los programas de optimización de antibióticos. El objetivo de este trabajo es la adaptación de la herramienta *Start Smart-Then Focus* al sistema de salud español.
Método: Se utilizó la metodología Delphi, mediante dos rondas de evaluación por correo electrónico. En la primera se envió un cuestionario con los criterios de la herramienta, estos fueron evaluados de forma independiente por 16 expertos. Puntuaron de 1-9 la idoneidad y aplicabilidad de cada criterio, y realizaron comentarios libres. La herramienta fue modificada y enviada de nuevo a todos los expertos, volvieron a puntuar individualmente, pero conociendo los resultados de la primera ronda.
Resultados: El primer cuestionario estaba constituido por 19 indicadores; 16 indicadores obtuvieron una mediana mayor de 7 en idoneidad y aplicabilidad, 3 indicadores obtuvieron mediana menor de 7 y 10 indicadores con mínimos menores de 5 en aplicabilidad. De 19 indicadores iniciales pasamos a 8; con 8 opciones dentro del sexto indicador.
Conclusiones: La adaptación de la herramienta *Start Smart-Then Focus* a nivel nacional puede ser de utilidad para implantarla en los programas de optimización de antibióticos y contribuir a la mejora del uso de los antimicrobianos.

PALABRAS CLAVE
Programas de optimización del uso de antimicrobianos; Antiinfecciosos; Resistencias antimicrobianas; Estudios de utilización de medicamentos; Indicadores de calidad de la atención de la salud.

Introduction

The spread of antimicrobial resistance is a worldwide problem. Among its causes is the inappropriate use of antimicrobials[1]. A recent strategy to improve their use is the implementation of antimicrobial stewardship programs (ASPs) in hospital and community environments[2-4]. Several studies have demonstrated the effectiveness of implementing ASP, as shown by improvements in antibiotic use, while others have reported reduced resistance and improved health outcomes, such as reductions in *Clostridioides difficile* infection, in bacteremia due to multidrug resistance, and in hospital-acquired candidemia[5-7].

However, the problem of increased resistance remains unresolved. For this reason, some health systems are developing other tools to be implemented in ASP. An example of this approach is the *Start Smart-Then Focus* (SStF) tool developed by the United Kingdom's National Health System (NHS)[8]. Following its implementation, the use of antimicrobials has improved in hospital and outpatient centres[9].

Tools developed in other health systems to improve the use of antimicrobials have to be adapted to the target health system in order to be implemented[10,11].

The objective of this study was to adapt the SStF tool to the Spanish health system through an expert panel consensus process.

Methods

A 4-person coordinating committee was formed, comprising members of the Spanish Society of Hospital Pharmacy, the Spanish Society of Infectious Diseases and Clinical Microbiology, the UK Pharmaceutical Society, and the European Society of Hospital Pharmacy. Subsequently, one of the pharmacists of the coordinating committee undertook a stay in a UK hospital to train in the management and implementation of the tool.

At the same time, an expert panel was formed to participate in the consensus process. The following selection criteria were applied: members of the panel had to be experts in ASP at a national level, specialists in hospital pharmacy, infectious diseases, microbiology, pediatrics, intensive or preventive medicine, or primary care pharmacists. The number of experts selected for each professional profile was based on the profiles of those most involved in ASP and the end users of this tool. The selection took into account the size and complexity of the centres where the experts worked. An initial panel of 18 experts was selected through Spanish national scientific societies and ASP groups. Of these, 17 experts accepted the invitation to participate, although only 16 completed both rounds of assessment.

Delphi methodology was used to reach consensus via two assessment rounds. In the first round, a questionnaire was sent to each member by e-mail. Each expert individually scored each item on suitability and applicability using a scale ranging from 1 to 9, where a score of 1 indicated complete disagreement, 5 indicated doubt, and 9 indicated complete agreement. Comments could also be added in each section.

Suitability was defined as follows: "The indicator corresponds to what is being measured".

Applicability was defined as follows: "It is feasible to implement the indicator in the centres".

In the second round, another questionnaire that had been modified according to the results of the first round was sent out. Each expert individually scored the items again, while aware of the anonymized results of the first round.

The scores obtained from the expert panel were analysed using the RAND/UCLA procedure[12].

Each criterion was classified as appropriate, inappropriate, or questionable based on median scores and the degree of disagreement.

Disagreement was defined according to the relationship between the interpercentile range (IPR) and the interpercentile range adjusted for symmetry (IPRAS). Disagreement on a given indicator was recorded when the IPR was higher than the IPRAS. The IPR was calculated as the difference between the 70th and 30th percentiles and the IPRAS according to the following formula: $IPRAS = 2.35 + 1.5 \cdot AI$, where AI is the asymmetry index, which represents the distance between the central point of the IPR and the central point (value 5).

The coordinating group was formed and the training stay began in May 2019.

The first mail-out and analysis of results took place in September and October 2019, and the second mail-out and final analysis took place in November and December 2019.

Results

Based on the SStF criteria, the Committee initially proposed the inclusion of 19 indicators within the questionnaire, 16 indicators in the clinical history or electronic prescription programs, and 3 indicators to audit and analyse the degree of adherence to the tool (Table 1). This questionnaire was sent out in the first round. The first column of table 1 contains the SStF criteria, the second column shows the indicators proposed by the coordinating group (numbered from 1 to 19), and the final column contains comments on them.

Table 1. First questionnaire sent to the expert panel:
INDICATORS TO BE DOCUMENTED IN THE CLINICAL HISTORY AND/OR ELECTRONIC PRESCRIPTION PROGRAM

Criteria START-SMART	Indicator to be included in the clinical history	Comments
Do not start antimicrobial therapy unless there is clear evidence of infection	1. Indication (reason for starting antimicrobial treatment)	If there is evidence of infection, there is an indication for antibiotic treatment (empirical or targeted treatment)
Take a thorough drug allergy history	2. If unconfirmed, confirm and record allergies	Allergy testing is needed when any prescription is made, whether for an antibiotic or another drug. If allergy suspected, it should be confirmed by requesting an allergy test
Initiate prompt effective antibiotic treatment within one hour of diagnosis (or as soon as possible) in patients with severe sepsis or life-threatening infections. Avoid inappropriate use of broad-spectrum antibiotics	3. Indication (in clinical history) and antibiotic prescription (in the electronic prescription program)	This indication would provide information on whether the patient had severe sepsis. The electronic prescription program should be consulted to know whether the right antibiotic has been administered within 1 hour
Comply with local antimicrobial prescribing guidance	4. Indication (in clinical history) and antibiotic prescription (in electronic prescription program)	Appropriate choice of antimicrobial agent according to local guidelines or reason given in clinical history for nonadherence to guideline recommendations

Table 1 ***(cont.).*** First questionnaire sent to the expert panel:
INDICATORS TO BE DOCUMENTED IN THE CLINICAL HISTORY AND/OR ELECTRONIC PRESCRIPTION PROGRAM

Criteria START-SMART	Indicator to be included in the clinical history	Comments
Document clinical indication (and disease severity if appropriate), drug name, dose and route on drug chart and in clinical notes	5. Indication (in clinical history) and antibiotic prescription (in electronic prescription program, including drug name, dose, and route)	The clinical history should state for which indication the antibiotics were prescribed The electronic prescription program must include the antibiotic/s to be prescribed, including dose and administration route
Include review/stop date or duration	None	Sometimes duration is not known a priori and so daily reviews must be conducted. This indicator is included later in FOCUS
Obtain cultures prior to commencing therapy where possible (but do not delay therapy)	6. Type of microbiological tests that have been requested	The clinical history must show which microbiological tests have been requested
Prescribe single dose antibiotics for surgical prophylaxis where antibiotics have been shown to be effective	7. Enter treatment duration in the electronic prescription program (such that antibiotic treatment is automatically discontinued). The electronic prescription program can also include prophylaxis protocols that allow a single dose as surgical antibiotic prophylaxis	The electronic prescription programs can be used to check how many doses have been prescribed
Document the exact indication on the drug chart (rather than stating long term prophylaxis) for clinical prophylaxis	8. Indication (in clinical history)	
Criteria FOCUS	**Indicator to be included in the clinical history**	**Comments**
Reviewing the clinical diagnosis and the continuing need for antibiotics at 48-72 hours and documenting a clear plan of action - the 'antimicrobial prescribing decision'	9. Review treatment daily and record decisions on antibiotic treatment in the patient's clinical history	All antimicrobial treatments should be reviewed daily
The five 'antimicrobial prescribing decision' options are:	Changed from 5 to 8 possible options for each antimicrobial treatment	
Stop antibiotics if there is no evidence of infection	10. Discontinue	Select the same indicator
Switch antibiotics from intravenous to oral	11. Switch to oral route	Select the same indicator
Change antibiotics – ideally to a narrower spectrum – or broader if required	12. Simplify treatment or scale up antimicrobial treatment (includes replacement with a broader-spectrum antibiotic or the addition of another antimicrobial)	Divided into two indicators: simplify and scale
Continue and document next review date or stop date	13. Continue (monitoring efficiency and safety)	Select the same indicator, adding that efficiency and safety should be monitored
Outpatient Parenteral Antibiotic Therapy (TADE)	14. Continue treatment via OPAT (Outpatient Parenteral Antibiotic Therapy)	Select the same indicator
	15. Dose adjustment (including monitoring levels)	New indicator
	16. Add duration	New indicator

Indicator used for auditing in the START, SMART, and FOCUS Methodology	PROPOSAL Indicators selected for auditing
Specific indication is documented on the prescription chart for ALL antibiotics	17. Is the indication documented in the clinical history and/or the electronic prescription program?
Antibiotic choice is in line with Trust guidelines OR culture and sensitivity results OR following the advice of a Consultant Microbiologist OR there is a justified reason for deviation from the guidelines	18. Is the treatment the most appropriate (according to centre-approved guidelines, microbiology results, and clinical situation of the patient)? Are the dose, route, and form of administration the most appropriate?
There is a stop or review date annotated on the prescription for ALL antibiotics *There is clear documentation of antibiotic review in the last 24 hrs in the medical notes* *For patients on antibiotic therapy for >3 days, there is a Day 3 Prescribing Decision clearly documented in the medical notes (Not applicable if on antibiotics for 3 days or less. Not applicable if on long term antibiotic prophylaxis)*	19. Have decisions on the antimicrobial treatment been recorded each day in the clinical history and/or electronic prescription program? There are 8 possible options: – Continue (monitoring efficacy and safety) – Discontinue – Simplify treatment – Scale up antimicrobial treatment (includes replacement with a broader-spectrum antibiotic or the addition of another antimicrobial) – Switch to oral route – Dose adjustment (including monitoring levels) – Add duration – Continue treatment via OPAT (Outpatient Parenteral Antimicrobial Therapy)

16 indicators had a median of more than 7 in suitability and applicability. Regarding applicability, 3 indicators had a median of less than 7 and 10 had a minimum of less than 5. The latter value coincided with those indicators on which the experts gave feedback on the difficulty of implementing them in their centres.

Table 2 shows the second questionnaire, after the tool had been modified based on previous comments and results. In this questionnaire, all changes have been underlined.

The second questionnaire was modified as follows:

- The order of the indicators was changed to facilitate the assessment of an antimicrobial treatment. The indicators on antibiotic prophylaxis were added at the end.
- Items that conveyed the same information were combined.
- The indicators used for auditing were deleted, and an indicator for analysing adherence to the tool as a whole was included in each criterion.
- Information was added to the criteria and to lower-scoring indicators.

From the initial 19 indicators, we obtained 8 final indicators. Eight options were added to the sixth indicator: "Review daily or at established intervals and record in the clinical history what decision is to be made regarding antibiotic treatment". In the second round, there were no disagreements and all the criteria and indicators were considered appropriate. However, there were doubts concerning one indicator: initiate prompt effective antibiotic treatment within 1 hour of diagnosis in patients with severe sepsis or life-threatening infections. Regarding applicability, only one indicator had a median of less than 7 and 5 indicators had a minimum of less than 5.

Table 2. Second questionnaire sent to the expert panel. INFORMATION TO BE DOCUMENTED IN THE CLINICAL HISTORY AND/OR ELECTRONIC PRESCRIPTION PROGRAM AND INDICATORS CONSTRUCTED WITH THIS INFORMATION FOR CONDUCTING AUDITS

Criteria START-SMART-FOCUS	Information to be included in the clinical history	INDICATOR	COMMENTS
Do not start antimicrobial therapy unless there is clear evidence of infection	1. Indication (reason for starting antimicrobial treatment)	Patient has an indication for antibiotic treatment: 1. YES 2. NO 3. INFORMATION UNAVAILABLE	
Take a thorough drug allergy history	2. Record allergies. If unconfirmed, make every effort to do so	Allergies are recorded: 1. YES 2. NO 3. INFORMATION UNAVAILABLE	This item has been reworded, because it is not possible to confirm allergies in all centres
Initiate prompt effective antibiotic treatment within one hour of diagnosis (or as soon as possible) in patients with severe sepsis or life-threatening infections. Avoid inappropriate use of broad-spectrum antibiotics	3. Indication with a ± severity scale (in clinical history) and antibiotic prescription (in electronic prescription program or other means according to service, centre, etc.)	If the patient has sepsis/septic shock or severe life-threatening infection Treatment has begun within 1 hour of diagnosis: 1. YES 2. NO 3. INFORMATION UNAVAILABLE	A +/- severity scale has been included because sometimes the indication alone is insufficient to know whether the infection is severe or not. It has also been documented that the prescription can be made by other means, because in emergency situations the prescription is sometimes requested verbally, making it necessary to check the prescription on patient charts, emergency charts, and so on, to be able to assess the time of administration. Subsequently, the prescription must be included in the electronic prescription programs
Comply with local antimicrobial prescribing guidance	4. Indication (in clinical history) and antibiotic prescription (in electronic prescription program)	Treatment is appropriate according to local guidelines, microbiological tests, or the patient's clinical situation: 1. YES 2. NO 3. INFORMATION UNAVAILABLE Are the dose, route, and form of administration the most appropriate? 1. YES 2. NO 3. INFORMATION UNAVAILABLE	
Obtain cultures prior to commencing therapy where possible (but do not delay therapy)	5. Type of microbiological tests requested and/or measures to control the outbreak (when needed)	The appropriate microbiological samples have been taken: 1. YES 2. NO 3. INFORMATION UNAVAILABLE If needed, have measures been established to control the outbreak? 1. YES 2. NO 3. INFORMATION UNAVAILABLE 4. N/A	This indicator was number 6 in the first questionnaire

Table 2 ***(cont.).*** Second questionnaire sent to the expert panel. INFORMATION TO BE DOCUMENTED IN THE CLINICAL HISTORY AND/OR ELECTRONIC PRESCRIPTION PROGRAM AND INDICATORS CONSTRUCTED WITH THIS INFORMATION FOR CONDUCTING AUDITS

Criteria START-SMART-FOCUS	Information to be included in the clinical history	INDICATOR	COMMENTS
Reviewing the clinical diagnosis and the continuing need for antibiotics at 48-72 hours and documenting a clear plan of action - the 'antimicrobial prescribing decision'	6. Review daily or at established intervals and record in the clinical history what decision is to be made regarding antibiotic treatment	The treatment is reviewed daily or according to established intervals: 1. YES 2. NO 3. INFORMATION UNAVAILABLE	This indicator was number 9 in the first questionnaire The possibility has been added of reviewing at established intervals (e.g. maintain treatment over the weekend if there are no changes and review again on Monday according to the results of imaging studies, cultures, etc). That is, if the patient is stable, the audit can be done in a more flexible way
Stop antibiotics if there is no evidence of infection	6.1. Discontinue		This indicator was number 10 in the first questionnaire
Switch antibiotics from intravenous to oral	6.2. Switch to oral route		This indicator was number 11 in the first questionnaire
Change antibiotics – ideally to a narrower spectrum – or broader if required	6.3. Simplify treatment		This indicator was number 12 in the first questionnaire
	6.4. Scale up antimicrobial treatment (includes replacement with a broader-spectrum antibiotic or the addition of another antimicrobial)		In the first questionnaire, this item was combined with item number 12: however, in the second questionnaire it is a new indicator
Continue and document next review date or stop date	6.5. Continue (monitoring efficiency and safety)		This indicator was number 13 in the first questionnaire
Outpatient Parenteral Antibiotic Therapy (TADE)	6.6. Continue treatment with OPAT if available at the centre		This indicator was number 14 in the first questionnaire The phrase "if available in the centre" has been added
	6.7. Dose adjustment (including level monitoring, if available at the centre)		This indicator was number 15 in the first questionnaire
	6.8. Add duration		This indicator was number 16 in the first questionnaire
		SURGICAL PROPHYLAXIS	
Document the exact indication on the drug chart (rather than stating long term prophylaxis) for clinical prophylaxis	7. Indication (in clinical history) and antibiotic prescription (in electronic prescription program)	Indication for antibiotic prophylaxis: 1. YES 2. NO 3. INFORMATION UNAVAILABLE Treatment is appropriate according to local guidelines, microbiological tests, or the patient's clinical situation: 1. YES 2. NO 3. INFORMATION UNAVAILABLE Are the dose, route, and form of administration the most appropriate? 1. YES 2. NO 3. INFORMATION UNAVAILABLE	
Prescribe single dose antibiotics for surgical prophylaxis where antibiotics have been shown to be effective	8. Add prophylactic treatment duration to the electronic prescription program (such that antibiotic treatment is automatically discontinued). The electronic prescription program can also include prophylaxis protocols that allow a single dose as surgical antibiotic prophylaxis	Antibiotic prophylaxis has been prescribed as a course of treatment or as a single dose 1. YES 2. NO 3. INFORMATION UNAVAILABLE	

Discussion

The present study describes the adaptation of the UK's NHS SStF tool to the Spanish health system. The final tool underwent several modifications based on an expert panel consensus process. Agreement was obtained among the experts and higher scores were obtained for suitability than for applicability.

To the best of our knowledge, this study is the first to adapt the UK's NHS SStF tool to another country. All published studies using this tool have been conducted in the UK[13,14].

A study similar to ours was recently conducted within the setting of the UK NHS using Delphi methodology[15]. Its objective was to design a tool to audit the suitability of antibiotic treatments based on SStF criteria. There were more participants in the expert panel than in our study, but fewer indicators were selected and they were not comparable to those used in our study.

There were no disagreements among the experts on any indicator and the suitability and applicability values were appropriate. However, there were doubts concerning the applicability of criterion 3 (initiate prompt effective antibiotic treatment within 1 hour of diagnosis in patients with severe sepsis or life-threatening infections). The reason underlying this exception is that it is currently very difficult to analyse this criterion using the information systems available.

The highest scores were obtained on suitability, showing that all the experts strongly agreed that the indicator was suitable: however, scores on applicability were somewhat lower. The indicators with lower applicability scores were as follows: to be able to confirm allergies, monitor plasma levels, and use outpatient parenteral antimicrobial therapy (OPAT) programs. Their applicability depends on the type of centre, infrastructure, and health service portfolio.

One of the strengths of this study is that the adapted tool includes indicators to audit implementation. Another strength is that it is based on a tool that has been validated in another country and implemented in many hospital and outpatient centres. It is also a pioneering study conducted in Spain and adapted by a panel of experts in ASPs at the national level.

The study has some limitations. The first concerns the selection of the expert panel. Although selection took place according to the inclusion criteria mentioned above, it only represents the professionals who will use the tool. Furthermore, the tool has not yet been validated in clinical practice, which represents the next phase of the study.

We suggest that it could be very useful to implement the Spanish adaptation of the SStF tool in Hospital and Primary Care ASPs and that it could prove to be an additional aid in improving the use of antimicrobials. To this end, a pilot study is needed and the indicators should be analysed over time to establish improvement strategies.

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Conflict of interest

No conflict of interest.

Contribution to the scientific literature

The *Start Smart-Then Focus* tool of the United Kingdom's National Health System (NHS) adapted to the Spanish national health system. The creation of a set of criteria that must be included in the patient's clinical history, along with quality indicators to assess the implementation of the tool and the appropriate use of antimicrobials.

This tool can be used in antibiotic optimization programs to determine the degree of appropriateness of antimicrobial use and establish improvement strategies.

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