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UNIVERSITÉ DE LORRAINE
2020

FACULTÉ DE MÉDECINE DE NANCY

THESE

Pour obtenir le grade de
DOCTEUR EN MEDECINE

Présentée et soutenue publiquement
dans le cadre du troisième cycle de Médecine Spécialisée

le 03/07/2020

par

Martin BELAN

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une revue systématique de littérature, les outils
disponibles et une enquête régionale des pratiques**

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SERMENT

« Au moment d'être admis à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité. Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux. Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions. J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité. Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l'humanité. J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences. Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences. Je donnerai mes soins à l'indigent et à quiconque me les demandera. Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

Admis dans l'intimité des personnes, je tairai les secrets qui me sont confiés. Reçu à l'intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs. Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l'indépendance nécessaire à l'accomplissement de ma mission. Je n'entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

J'apporterai mon aide à mes confrères ainsi qu'à leurs familles dans l'adversité.

Que les hommes et mes confrères m'accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonoré et méprisé si j'y manque ».

LISTE DES ABREVIATIONS

ABS	Antibiotic stewardship
AMR	Antimicrobial resistance
BLSE	Béta-lactamase à spectre élargi
BMR	Bactérie multi-résistante
CDC	Center for disease control and prevention
DDD	Daily defined dose
EBLSE	Entérobactérie productrice de béta-lactamase à spectre élargi
ECDC	European center for disease prevention and control
ECBU	Examen cytobactériologique des urines
EHPAD	Établissement d'hébergement pour personnes âgées dépendantes
EPC	Entérobactérie productrice de carbapénémase
ERG	Entérocoque résistant aux glycopeptides
ETP	Équivalent temps plein
EU/EEA	European union/European economic area
FTE	Full time equivalent
GIR	Groupe iso-ressources
GP	General practitioner
ID	Infectious diseases
INSEE	Institut national de la statistique et des études économiques
KPC	Klebsiella pneumoniae carbapenemase
NH	Nursing home
PLP2a	Protéine de liaison à la pénicilline 2a
RR	Risque relatif
SARM	Staphylococcus aureus résistant à la méticilline

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INTRODUCTION

1. Antibiorésistance

1.1. Définition – Historique

Les antibiotiques sont des substances d'origine synthétique ou naturelle utilisées pour lutter contre les infections causées par les bactéries. Le premier antibiotique à avoir été utilisé en pratique clinique est la pénicilline découverte en 1928 par Alexander Fleming, objet de son prix Nobel de 1945 et dont l'utilisation en pratique clinique a débuté à partir de 1941 [1]. Leur découverte a permis une évolution vers la médecine moderne et a fait drastiquement chuter la mortalité liée aux maladies infectieuses. Alors qu'il s'agissait en France de la première cause de mortalité en 1940, les maladies bactériennes ne sont aujourd'hui responsables que de 2% des décès en France [2]. Une étude américaine s'intéressant aux variations de la mortalité liée aux maladies infectieuses aux États-Unis au XXe siècle a mis en évidence un déclin annuel des décès par maladies infectieuses plus marqué entre 1938 et 1952 (8,2% vs 2-3% pour les périodes 1900-1937 et 1953-1980), principalement dû à la diminution de la mortalité imputable aux pneumonies, aux complications bactériennes de la grippe et à la tuberculose, coïncidant avec les premières utilisations de la pénicilline, des sulfonamides et de la streptomycine [3].

Cependant l'utilisation d'un antibiotique en pratique clinique s'accompagne systématiquement de l'émergence de résistances bactériennes. Concernant la pénicilline, dès 1940, des souches d'*Escherichia coli* capable d'inactiver la pénicilline par la production d'une pénicillinase étaient décrites. Des souches de *Staphylococcus aureus* résistantes à la pénicilline étaient également décrites dès 1942 et à la fin des années 1960, 80% des souches de *Staphylococcus aureus* hospitalières et communautaires étaient résistantes à la pénicilline [4]. L'apparition rapide de résistances aux antibiotiques a été décrite pour chaque antibiotique dans les années qui ont suivi sa mise sur le marché (Tableau 1).

Tableau 1. Apparition des résistances bactériennes après l'introduction sur le marché des antibiotiques (CDC, 2020) [5]

Antibiotic Approved or Released	Year Released	Resistant Germ Identified	Year Identified
Penicillin	1941	Penicillin-resistant <i>Staphylococcus aureus</i>	1942
		Penicillin-resistant <i>Streptococcus pneumoniae</i>	1967
		Penicillinase-producing <i>Neisseria gonorrhoeae</i>	1976
Vancomycin	1958	Plasmid-mediated vancomycin-resistant <i>Enterococcus faecium</i>	1988
		Vancomycin-resistant <i>Staphylococcus aureus</i>	2002
Amphotericin B	1959	Amphotericin B-resistant <i>Candida auris</i>	2016
Methicillin	1960	Methicillin-resistant <i>Staphylococcus aureus</i>	1960
Extended-spectrum cephalosporins	1980 (Cefotaxime)	Extended-spectrum beta-lactamase-producing <i>Escherichia coli</i>	1983
Azithromycin	1980	Azithromycin-resistant <i>Neisseria gonorrhoeae</i>	2011
Imipenem	1985	<i>Klebsiella pneumoniae</i> carbapenemase (KPC)-producing <i>Klebsiella pneumoniae</i>	1996
Ciprofloxacin	1987	Ciprofloxacin-resistant <i>Neisseria gonorrhoeae</i>	2007
Fluconazole	1990 (FDA approved)	Fluconazole-resistant <i>Candida</i>	1988*
Caspofungin	2001	Caspofungin-resistant <i>Candida</i>	2004
Daptomycin	2003	Daptomycin-resistant methicillin-resistant <i>Staphylococcus aureus</i>	2004
Ceftazidime-avibactam	2015	Ceftazidime-avibactam-resistant KPC-producing <i>Klebsiella pneumoniae</i>	2015

*autorisation de mise sur le marché en 1990 aux États-Unis mais déjà utilisé en pratique clinique dans les années précédentes

1.2. Mécanismes de l'antibiorésistance

La résistance aux antibiotiques est ancienne et est le résultat attendu de l'interaction entre de nombreux micro-organismes dont la plupart synthétisent naturellement des substances antimicrobiennes, conduisant à l'acquisition par les bactéries de mécanismes de défense pour assurer leur survie. On distingue classiquement les résistances naturelles d'une bactérie, qui font partie de ses caractéristiques propres et existent chez toutes les souches d'une espèce, des résistances acquises. C'est ce second type de résistance qui a un impact en pratique clinique par l'acquisition (et la transmission éventuelle) de résistance aux antibiotiques chez des bactéries antérieurement sensibles. Les 4 principaux mécanismes de résistances aux antibiotiques sont :

- La résistance enzymatique (exemple : production d'une pénicillinase chez *Staphylococcus aureus* inhibant l'action de la pénicilline A)
- La modification de cible (exemple : acquisition de la PLP2a codée par le gène *mecA* chez *Staphylococcus aureus* entraînant une résistance à la méticilline (SARM))
- L'efflux (exemple : acquisition d'un système d'efflux MexA-MexB-OprM chez *Pseudomonas aeruginosa* entraînant une résistance à la ticarcilline et l'aztréonam)
- L'imperméabilité (exemple : perte de la porine D2 par mutation chez *Pseudomonas aeruginosa* entraînant une résistance à l'imipénème)

Ces mécanismes de résistance existent de manière variable chez l'ensemble des bactéries et peuvent s'acquérir soit par mutation, soit par transfert horizontal de matériel génétique (plasmide, transposon, intégron)[6].

Les 2 principaux déterminants de l'émergence et de la propagation de la résistance bactérienne acquise sont [7]:

- L'utilisation des antibiotiques, qui exercent une pression écologique sur les bactéries et contribuent à l'émergence et à la sélection de populations bactériennes résistantes aux antibiotiques ;
- La propagation et la transmission croisée des bactéries résistantes aux antibiotiques entre humains, entre humains et animaux, et entre humains/animaux et environnement.

Le lien entre consommation d'antibiotiques et résistance bactérienne est bien démontré puisque qu'à l'échelle d'une population le niveau de consommation d'antibiotiques est corrélé avec le niveau d'antibiorésistance [7]. Une étude européenne de 2005 s'est intéressée à la relation entre consommation d'antibiotiques en ville et résistance bactérienne au niveau des pays. Il y avait été mis en évidence une association positive notamment entre la prescription de pénicilline et l'émergence de pneumocoque de sensibilité diminuée à la pénicilline, mais également la prescription de ciprofloxacine et cotrimoxazole responsable d'émergence de résistance chez *E. coli* [8]. Les auteurs constataient que la prévalence de l'antibiorésistance était plus élevée dans les pays de l'Europe de l'Est et du Sud où les consommations d'antibiotiques étaient généralement plus importantes que dans les pays d'Europe du Nord (cf. figures 1,2,3 et 4). Des associations statistiquement significatives entre utilisation et résistance à un antibiotique ont également été mises en évidence en milieu hospitalier [9,10].

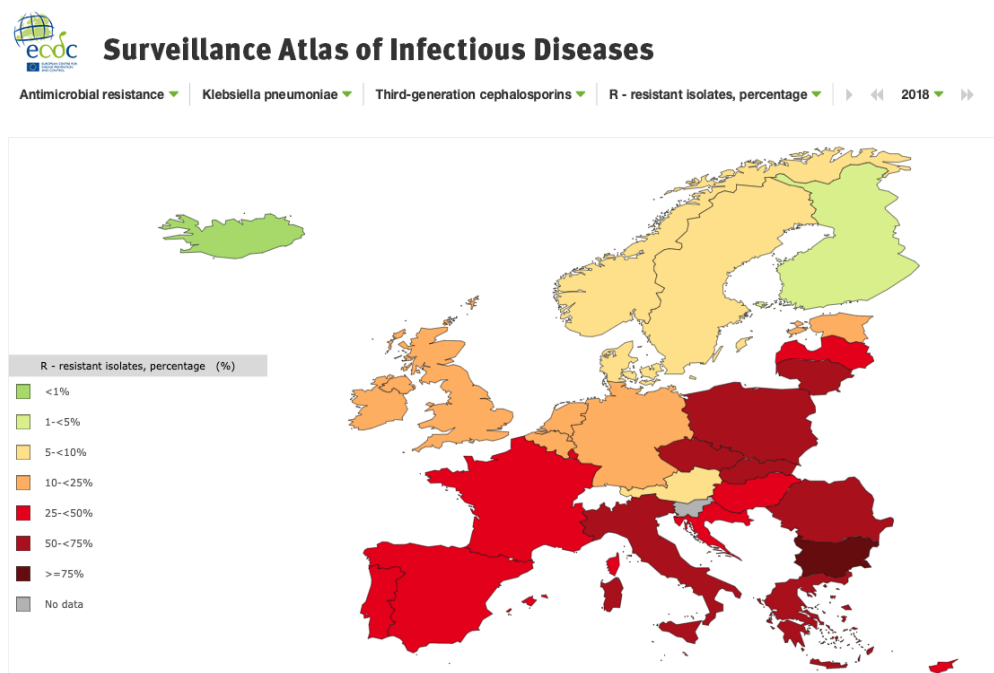
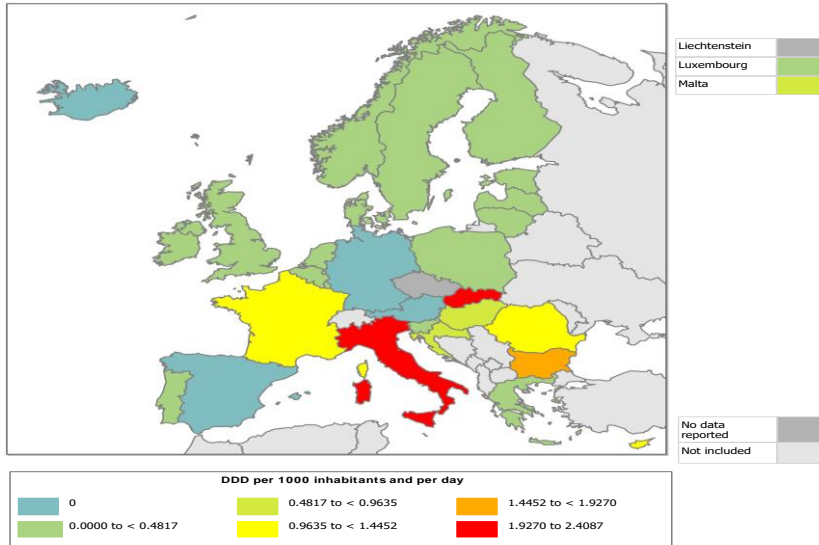


Figure 1. Taux de *Klebsiella pneumoniae* (en % d'isolats cliniques) résistantes aux céphalosporines de 3ème génération en Europe, 2018 (données ECDC)

Geographical distribution of the consumption of Third-generation cephalosporins (ATC group J01DD) in the community and hospital sector in Europe, reporting year 2018

* No data are shown for those countries only reporting data for the community

Consumption of Third-generation cephalosporins (ATC group J01DD) in the community and hospital sector in Europe, reporting year 2018



This report has been generated from ESAC-Net data submitted to TESSy, The European Surveillance System on 2020-06-07. The report reflects the state of submissions in TESSy as of 2020-06-07 at 17:00

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Figure 2. Distribution de la consommation de céphalosporines de 3^{ème} génération en Europe, 2018 (en DDD/100 000 habitants/an) (données ECDC)

Surveillance Atlas of Infectious Diseases

Antimicrobial resistance ▾ Escherichia coli ▾ Fluoroquinolones ▾ R - resistant isolates, percentage ▾ 2018 ▾

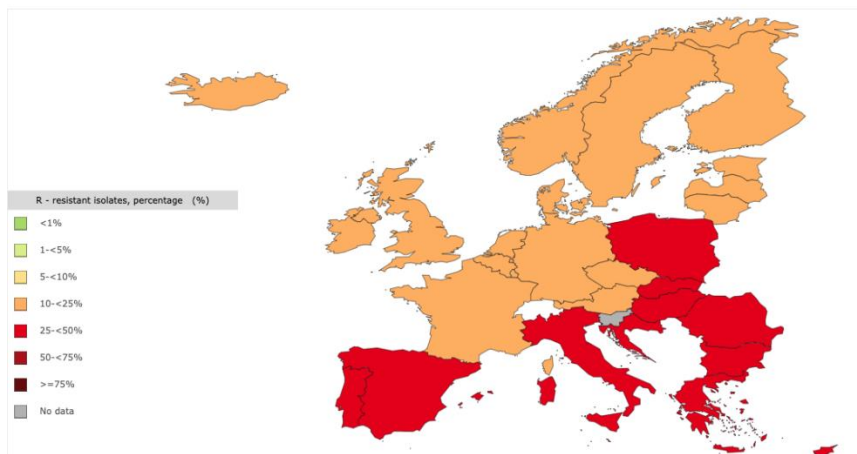
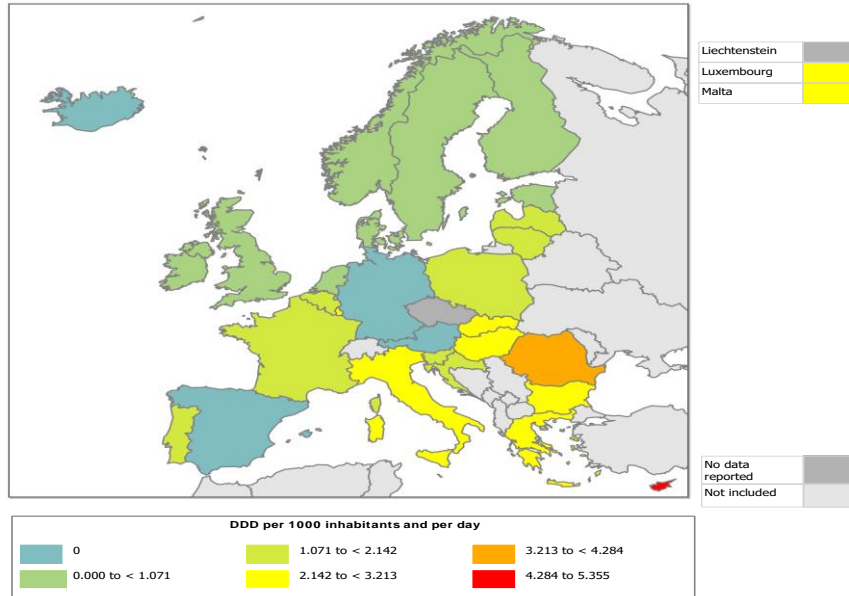


Figure 3. Taux de *Escherichia coli* (en % d'isolats cliniques) résistants aux fluoroquinolones en Europe, 2018 (données ECDC)

Geographical distribution of the consumption of Fluoroquinolones (ATC group J01MA) in the community and hospital sector in Europe, reporting year 2018

* No data are shown for those countries only reporting data for the community

Consumption of Fluoroquinolones (ATC group J01MA) in the community and hospital sector in Europe, reporting year 2018



This report has been generated from ESAC-Net data submitted to TESSy, The European Surveillance System on 2020-06-07. The report reflects the state of submissions in TESSy as of 2020-06-07 at 17:00

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Figure 4. Distribution de la consommation de fluoroquinolones en Europe, 2018 (en DDD/100 000 habitants/an) (données ECDC)

1.3. Conséquences

Non seulement, l'émergence de la résistance aux antibiotiques est responsable d'infections plus difficiles à traiter, nécessitant des molécules souvent plus chères et plus toxiques, et des durées d'hospitalisation plus longues, mais l'antibiorésistance pourrait également menacer les avancées de la médecine moderne notamment la réalisation de certaines chirurgies ou chimiothérapies anticancéreuses.

Au niveau individuel, la colonisation par une bactérie multi-résistante (BMR) augmente le risque de développer une infection à cette bactérie résistante. Une méta-analyse de 2017 s'intéressant à la colonisation à Entérobactérie productrice de Beta-Lactamase à Spectre Élargi (EBLSE) montrait que le risque d'infection à EBLSE était presque 50 fois supérieurs chez les patients colonisés au niveau digestif comparé aux patients non colonisés [11]. De même, concernant les entérobactéries productrices de carbapénémase (EPC), une revue systématique de littérature américaine publiée en 2016 étudiant le risque d'infection à EPC rapportait que 16,5% des patients colonisés à EPC présentaient dans les suites une infection à EPC dont il était rappelé que la mortalité est proche de 50% [12].

En terme de santé publique, d'après une étude européenne publiée par Cassini *et al.*, le nombre d'infections à bactéries multi-résistantes d'intérêt médical était estimé à plus de 670 000 sur l'année 2015 dont 33 000 décès [13]. Parmi ces chiffres, la France comptait 124 000 infections à bactéries multi-résistantes et 5 500 décès associés, soit 1/6^{ème} des infections et des décès. Les chiffres américains sont à peu près similaires aux chiffres européens avec 35 000 décès/an. Le coût estimé de l'antibiorésistance pour les systèmes de santé des pays européens est évalué à 1.1 milliards d'euros [14]. D'ici 2050, le nombre de décès imputables aux bactéries multirésistantes pourrait atteindre 10 millions et le coût associé pourrait atteindre les cent mille milliards de dollars [15]. Pour toutes ces raisons, la résistance aux antibiotiques fait partie de la liste des 10 menaces qui pèsent sur la santé mondiale en 2019 selon l'Organisation Mondiale de la Santé [16], et de nombreux plans d'actions nationaux et internationaux ont été mis en place pour lutter contre l'antibiorésistance, incluant notamment les stratégies de bon usage des antibiotiques.

2. Bon usage des antibiotiques

2.1. Définition et stratégies

La notion de bon usage des antibiotiques est initialement apparue aux États-Unis dans les années 1990 sous l'expression *Antimicrobial stewardship* en utilisant un terme qui intégrait à la fois la notion de l'utilisation appropriée des antibiotiques lorsque ceux-ci sont indiqués, et d'éviter les prescriptions inutiles d'une ressource non-renouvelable à l'infini dans un contexte d'antibiorésistance croissante [17]. Le bon usage des antibiotiques a été défini dans un article publié en 2017 par Dyar *et al.* comme un ensemble cohérent de mesures conçues pour utiliser les antibiotiques de façon responsable [18]. Cette définition permet d'aborder les deux objectifs du bon usage des antibiotiques qui sont 1) d'assurer un traitement optimal et efficace pour les patients atteints d'infection bactérienne et 2) de minimiser les effets collatéraux de la prescription d'antibiotiques (effets secondaires, infection à *Clostridioides difficile*, émergence de BMR). Elle englobe également à la fois la médecine humaine et vétérinaire.

Le bon usage des antibiotiques correspond actuellement à un grand nombre de stratégies hétérogènes qui sont habituellement classées en 2 catégories : les stratégies restrictives d'une part, par exemple les antibiogrammes ciblés, les formulaires de prescription et la validation de prescription par des spécialistes ou l'arrêt automatique de reconduction des prescriptions ; et les stratégies incitatives, respectant la liberté des prescripteurs d'autre part, comme la formation des professionnels par différents supports, l'utilisation d'aides informatisées à la décision ou les audits avec retour d'information (feedback).

En France, la feuille de route interministérielle pour maîtriser la résistance bactérienne aux antibiotiques de 2016 intègre ces stratégies de bon usage des antibiotiques pour diminuer les consommations et ralentir la progression des résistances bactériennes aux antibiotiques. Au niveau mondial, le plan d'action global One Health AMR mené par l'Organisation Mondiale de la Santé vise également à combattre l'antibiorésistance par le développement et la mise en place de programmes de bon usage des antibiotiques.

2.2. Effets des programmes de bon usage des antibiotiques

Les stratégies de bon usage des antibiotiques se sont d'abord intéressées au milieu hospitalier, ce qui explique que la majorité des études aient été réalisées dans ce secteur. Plusieurs méta-analyses s'intéressant à ces études ont récemment été publiées confirmant l'impact positif des programmes de bon usage des antibiotiques sur des critères de jugement cliniques et microbiologiques. Schuts *et al.* ont publié en 2016 une méta-analyse s'intéressant aux effets des différentes composantes des programmes de bon usage des antibiotiques sur la mortalité, les durées de séjour et les effets secondaires des antibiothérapies [19]. Il a notamment été montré qu'une antibiothérapie probabiliste adaptée aux recommandations ou la désescalade d'une antibiothérapie après documentation microbiologique permettait une réduction relative du risque de mortalité respectivement de 35% et 56% dans les groupes « intervention » ou que le déplacement au lit du patient d'un infectiologue permettait une réduction relative du risque de mortalité de 66% dans le cadre des bactériémies à *Staphylococcus aureus*. Baur *et al.* cherchaient à déterminer dans leur méta-analyse qui incluait 32 études si les programmes de bon usage pouvaient réduire les colonisations ou infections à BMR et les infections à *Clostridioides difficile* ; ils ont montré une réduction de 51% des infections et colonisations à Bacilles gram négatif multirésistants , 48% pour les entérobactéries BLSE, 37% pour les *Staphylococcus aureus* résistants à la méticilline et une réduction de 32% des infections à *Clostridioides difficile*, bien que ces résultats soient à interpréter avec précautions du fait de l'hétérogénéité des études incluses [20]. Ces programmes ont montré un impact dans les services d'onco-hématologie, de réanimation et de médecine et l'effet était d'autant plus important qu'ils étaient associés à des mesures de prévention et contrôle des infections. Enfin, Davey *et al.* ont montré dans leur revue Cochrane que la mise en place de programmes de bon usage des antibiotiques était associée à une diminution de la durée de prescription d'antibiotiques (-1,95j), une diminution de la durée moyenne d'hospitalisation et qu'il n'y avait pas d'augmentation de la mortalité dans les groupes intervention [21].

Des résultats similaires sur les consommations d'antibiotiques, toujours sans effet délétère pour les patients, ont pu être mis en évidence dans le cadre des soins primaires en utilisant des stratégies de bon usage adaptées aux prises en charge en ville (éducation aux recommandations, utilisation de tests diagnostiques rapides au cabinet, entraînement à la

communication avec les patients, ordonnance de non prescription) mais sans qu'il n'y ait eu d'effet rapporté sur les colonisations à BMR des patients [22].

3. Problématique des EHPAD

3.1. *Caractéristiques des EHPAD*

Les EHPAD ou Établissements d'Hébergement pour Personnes Âgées Dépendantes sont des établissements dédiés à l'accueil des personnes âgées de plus de 60 ans en situation de perte d'autonomie physique et/ou psychique et qui nécessitent une aide pour les activités de vie quotidienne ainsi que des soins médicaux avec un personnel dédié disponible 24/24h [23].

Selon l'INSEE, en France, fin 2016, on comptait 7 438 établissements de type EHPAD avec un total de 605 000 places d'hébergement [24]. Un rapport de la Direction de la Recherche, des Études, de l'Évaluation et des Statistiques de 2015 rapportait un nombre de 585 560 résidents en EHPAD fin 2015 dans des établissements privés à but lucratif, privés à but non lucratif et publics. La moitié de ces résidents étaient âgés de plus de 87,5 ans et le niveau de dépendance y était en augmentation par rapport à 2011 avec 54% des résidents d'EHPAD ayant un score GIR évalué à 1 ou 2 [25]. Une étude française portant sur 25 500 nouveaux résidents a étudié les pathologies dont étaient atteintes les résidents entrant en EHPAD au cours du premier trimestre de l'année 2013 : près d'un nouveau résident sur deux (48%) avait été pris en charge pour une pathologie cardio-vasculaire au cours de l'année précédente, 40% pour une pathologie neurodégénérative (incluant les démences) et 18% et 17% respectivement pour un cancer ou un diabète [26]. En plus de ces nombreuses comorbidités associées à une polymédication, les résidents d'EHPAD sont porteurs d'un certain nombre de dispositifs médicaux comme les cathéters vasculaires ou sondes urinaires, respectivement 3.3% et 1.7% dans une enquête de prévalence des infections associées aux soins en EHPAD menée en 2016 [27].

Concernant le personnel des EHPAD, fin 2015, en France, le taux d'encadrement pour 100 places dans les EHPAD était de 5,8 ETP pour les infirmiers, 20,7 pour les aides-soignants et 0,4 pour les médecins coordonnateurs, ce qui était en progression par rapport à 2011 [28]. Cependant 44,1% des établissements répondants déclaraient avoir des difficultés de

recrutement, et notamment 10% déclaraient avoir un poste de médecin coordonnateur non pourvu et ce chiffre était de 9,2% pour les postes d'aides-soignants. Ces difficultés de recrutement de personnel sont associées également à un turn-over important des équipes. Il est à noter que le nombre de médecins généralistes intervenant dans les EHPAD est important, 12 en moyenne [27].

3.2. *Problèmes de l'antibiothérapie et de l'antibiorésistance dans les EHPAD*

La problématique des bactéries multirésistantes aux antibiotiques (BMR) touche également les EHPAD que ce soit en termes de colonisation ou d'infection. Dans l'enquête de prévalence des infections associées aux soins Prév'EHPAD réalisée en 2016-2017 dans 367 EHPAD en France, sur les 233 micro-organismes isolés dans les ECBU réalisés, 26,3% des entérobactéries isolées étaient résistantes aux céphalosporines de 3^{ème} génération, dont 13.3% de souches productrices de BLSE [27]. Des résultats similaires ont été trouvés en Belgique dans une étude réalisée en 2015 dans 29 établissements rapportant des taux de colonisation des résidents de 9% à SARM, 11% à BLSE et moins de 0,1% à Entérocoque Résistant aux Glycopeptides (ERG) ou Entérobactérie Productrice de Carbapénémase (EPC) [29]. Une méta-analyse publiée en 2017, dont la majorité des études incluses étaient américaines, calculait une prévalence moyenne de colonisation à bacilles gram négatifs BMR à 27% chez des résidents d'EHPAD [30].

Cette prévalence importante de BMR chez les résidents d'EHPAD est en partie expliquée par l'utilisation importante, et parfois abusive, des antibiotiques dans ces établissements. 2,7% des patients inclus dans l'enquête Prév'EHPAD recevaient une antibiothérapie le jour de l'enquête dont 13.7% à visée prophylactique avec une durée moyenne de 176 jours [27]. L'enquête européenne de prévalence HALT-3 réalisée en 2016-2017 et s'intéressant aux infections associées aux soins et aux prescriptions d'antibiotiques montrait que 4.9% des résidents d'EHPAD recevaient un traitement par antibiotique le jour de l'enquête avec d'importantes variations entre pays (0,7% pour la Lituanie à 10,5% pour l'Espagne ou le Danemark) dont environ un tiers était à visée prophylactique. Selon le *Center for Disease Control and Prevention (CDC)* aux États-Unis, jusqu'à 70% des résidents en

EHPAD reçoivent un traitement antibiotique chaque année et 40% à 75% de ces prescriptions sont inappropriées ou inutiles ; le CDC recommande donc l'application de son programme de bon usage des antibiotiques spécifiquement conçu pour les EHPAD [31].

OBJECTIFS

Les objectifs de ce travail étaient de :

- 1- Faire une revue systématique de littérature des études interventionnelles étudiant les effets des programmes de bon usage des antibiotiques mis en place dans des EHPAD ;
- 2- Lister de façon aussi exhaustive que possible les outils disponibles gratuitement sur internet ayant pour objectif d'aider à la mise en place de ces programmes dans les EHPAD ;
- 3- Connaître les stratégies déjà mises en place dans les EHPAD du Grand Est pour favoriser le bon usage des antibiotiques et évaluer l'acceptabilité de diverses interventions par le biais d'une enquête régionale.

ARTICLE 1 : ANTIMICROBIAL STEWARDSHIP PROGRAMMES IN NURSING HOMES : A SYSTEMATIC REVIEW AND INVENTORY OF TOOLS

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Antimicrobial stewardship programmes in nursing homes: a systematic review and inventory of tools

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Background: Antimicrobial overuse/misuse is common in nursing homes and although the effectiveness of antimicrobial stewardship (AMS) programmes has been well explored and demonstrated in hospitals, data are scarce for the nursing-home setting. Our objectives for this systematic review were to make an inventory of: (i) all interventions that could be considered as part of AMS programmes in nursing homes; and (ii) all stewardship tools and guidance that are freely available.

Methods: We performed a systematic review using the MEDLINE database from inception to June 2018, including all interventional studies, reviews, opinion pieces and guidelines/guidance exploring AMS programmes in nursing homes. For the inventory of freely available tools and guidance to help implement an AMS programme, we also performed screening of professional societies and official agencies' websites and a questionnaire survey among a panel of international experts.

Results: A total of 36 articles were included in our systematic review. Most interventions took place in North America and have explored education or persuasive interventions within multifaceted interventions, showing that they can improve guideline adherence and decrease antibiotic use and unnecessary microbiological testing. Most reviews also highlighted the importance of accountability, monitoring and feedback. A large number of tools (156) available for free on the internet were identified, mostly about education, patient assessment and outcome measurement.

Conclusions: Although high-quality interventional studies are lacking, multifaceted interventions including education, monitoring and feedback seem the most promising strategy. Many tools are available on the internet and can be used to help implement AMS programmes in nursing homes.

Introduction

Antimicrobial resistance (AMR) was included by the WHO on the list of the 10 threats to global health in 2019.¹ In order to tackle this threat, antimicrobial stewardship (AMS), defined by a coherent set of actions designed to use antimicrobials responsibly, is needed in all settings.²

The positive impact of AMS programmes in hospitals has been well established to reduce antimicrobial use, to improve patient outcomes (reduction of infections or colonizations with MDR organisms) and to reduce costs, but evidence is still scarce in other settings such as nursing homes (NHs).^{3–5}

Antimicrobial use is high in NHs, as demonstrated by several point prevalence surveys, with up to 15% of residents receiving at least one antimicrobial course on the day of the survey and 47%–78% receiving at least one antimicrobial course per year.^{6–8} More than half of these prescriptions are considered inappropriate

or unnecessary.^{9,10} This contributes to a high prevalence of MDR organisms and other antibiotic-related adverse events, such as *Clostridioides difficile* infections.^{11,12}

In the USA, NHs have been required to have 'an antibiotic stewardship program that includes antibiotic use protocols and a system to monitor antibiotic use' since 2017.¹³ In Europe, the ECDC issued guidelines in 2017 for the prudent use of antimicrobials in human medicine, recommending that NHs should implement AMS programmes.¹⁴ However, no clear guidelines are available to guide the implementation of such programmes in NHs, except for the CDC core elements of antibiotic stewardship for NHs.¹⁵

Our objectives were: (i) to perform a systematic review including all interventional studies, reviews, opinion pieces and guidelines/guidance exploring AMS in NHs; and (ii) to make an inventory of freely available tools useful for implementing an AMS programme in NHs.

Methods

Data sources and search strategy

For the systematic literature review, we searched the MEDLINE database (without any language restriction) and included articles from inception to June 2018 inclusive, using the following keywords: (antibiotic OR antimicrobial) AND (stewardship OR intervention OR program) AND (long term care OR nursing home OR LTCF) (LTCF: long-term care facility).

For the inventory of tools, we extracted freely available resources found in the articles included in the systematic review. In addition, we conducted a questionnaire survey among a panel of international AMS experts (convenience sample selected by C.P.). This survey consisted of a short two-item questionnaire asking the international panel of experts whether they were aware of any recommendations or guidelines for AMS implementation in NHs and whether they knew any tools that could be used for such an AMS programme. Our inventory was completed by an internet search including leading international organizations, professional societies and non-governmental organizations' websites (WHO, CDC, ECDC, BSAC, Société de Pathologie Infectieuse de Langue Française, Antimicrobial Resistance Australia, ESCMID, ReAct – Action on Antibiotic Resistance, Center for Disease Dynamics Economics & Policy and Center for Infectious Disease Research and Policy) and explored any links on these websites that could be related to AMS in NHs. All these websites were explored using the websites' navigation menus and search boxes and the following keywords: 'antimicrobial stewardship' and 'nursing home'.

Study/tools selection

Regarding the systematic review, we included all interventional studies and reviews assessing the impact of an AMS programme or intervention for elderly people/residents living in the NH setting. We also included guidelines/guidance and expert-opinion articles focusing on AMS in NHs. We did not include observational studies or studies performed in residential LTCFs or specialized LTCFs (e.g. rehabilitation care, intensive care, psychiatric care). Based on the definition provided by the 2013 ECDC point prevalence survey of healthcare-associated infections and antimicrobial use, we used the following definitions for NHs: 'institutions where elderly stay temporarily or permanently. The residents in these NH need medical and/or skilled nursing care and supervision 24 h per day'.¹⁶ We also defined residential LTCFs, where 'residents are unable to live independently' and 'require supervision and assistance for the activities of daily living' and specialized LTCFs, which 'are specialized in one specific type of care, for example, physical impairment, chronic diseases such as multiple sclerosis, dementia, psychiatric illnesses, rehabilitation care, palliative care, etc.' based on this survey. Two junior researchers (M.B. and Francesca Binda) independently performed screening of the literature based on titles and abstracts to select articles meeting the inclusion criteria and discussed their results. M.B. read the full text of the selected articles to decide on their inclusion. In case of doubt or discrepancy, a senior researcher (N.T. or C.P.) was consulted.

Tools were included in our inventory if they were both available for free and dealt with the implementation of an AMS programme in NHs.

Quality assessment

Our systematic review complies with the preferred reporting items for systematic review and meta-analysis (PRISMA) reporting guidelines.¹⁷ For each included interventional study, we assessed the level of evidence, based on the study design, and extracted relevant information such as design, setting, type of intervention and outcomes. We used the Mulrow criteria to assess the quality of the included systematic reviews.¹⁸ No quality assessment was made for other types of articles (e.g. narrative reviews or opinion pieces).

Data synthesis

We categorized the retrieved items using the global core elements for AMS categories recently published by an international panel of experts.¹⁹

Results

Systematic literature review

A total of 3621 articles were identified. After the first screening, based on titles and abstract, 54 articles were selected for full-text reading. We finally included 36 articles meeting the inclusion criteria (Figure 1).

Among these articles, 18 were interventional studies evaluating AMS interventions in NHs, with 5 of them being randomized controlled studies, 7 quasi-experimental before-after controlled studies and 6 before-after uncontrolled studies. Most studies took place in the USA ($n=12$; including one in both the USA and Canada) and the others were conducted in Canada ($n=2$), the Netherlands, Sweden, Finland and the UK ($n=1$ each). Almost all ($n=15$) implemented a multifaceted intervention and only 3 used only one type of core element (Available expertise on infection management, Other actions: guidelines or patient assessment form).^{20–22} Among the 15 multifaceted interventions, 14 included an educational component and 12 included an 'other action' component (creation of local guidelines, diagnosis or microbiology testing algorithms, use of information technology, antibiograms or patient assessment forms).

The outcomes evaluated by these studies were overall or specific antimicrobial use, guideline-adherent prescriptions, microbiology testing and decrease in unnecessary antimicrobial use (e.g. urinary tract infection prophylaxis or asymptomatic bacteriuria treatment).^{23,24} The impact of the studied intervention reached statistical significance for specific outcomes in some studies only (Table 1), but all but one described an improvement in at least one outcome.²⁵

Eight systematic reviews and nine expert opinions were also included, as well as two guidelines/guidance documents (Table 1).

The interventions we identified overall spanned the whole range of AMS core elements (Table 1).

Further information on the articles included in our review is presented in Tables S1 and S2 (available as [Supplementary data at JAC Online](#)).

Inventory of tools and guidance

Regarding the questionnaire survey of international experts, we obtained a 57.4% response rate, with 31/54 experts from 21 middle-to-high-income countries (Argentina, Austria, Belgium, Canada, Croatia, France, Germany, Greece, Ireland, Italia, Malta, the Netherlands, Luxembourg, Norway, Poland, Portugal, Serbia, Spain, Sweden, Turkey and the UK) replying to our survey.

Our internet search focused on the 10 websites of leading international organizations, professional societies and non-governmental organizations described in the Methods section and led to 14 additional websites being explored [Agency for Healthcare Research and Quality (AHRQ); National Centre for Antimicrobial Stewardship; Alberta Health Services; Association of Medical Microbiology and Infectious Disease Canada; Minnesota Health Department; Observatoires des Médicaments, Dispositifs

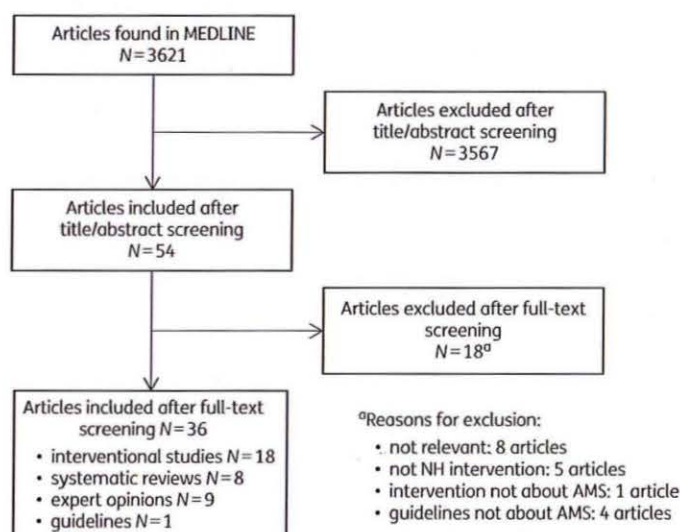


Figure 1. Flow chart of the systematic review of the literature.

médicaux et Innovations thérapeutiques Bretagne; University of Rochester; Saskatchewan Health Authority; Arizona Department of Health; Nebraska Antimicrobial Stewardship Assessment and Promotion Program; Infectio-Lille; the NHS; Michigan Antibiotic Resistance Reduction coalition; and Washington State Department of Health).

A total of 156 tools freely available on the internet were found from the website search and the questionnaire survey, with six additional tools extracted from the literature review (Table 2). They were all created between 2008 and 2019, with more than half of them being created in the last 3 years. The vast majority of resources were found on national or regional agencies from the USA, with some resources coming from Canada, Australia, the UK and France.

More than a third of them were educational materials ($n=58$), mostly targeting health professionals ($n=41$), while others were for the education of residents and relatives. One-third ($n=58$) belonged to the 'other actions aiming at responsible antimicrobial use' category, including diagnosis/algorithms, assessment/communication tools, microbiology testing and antibiograms. We did not identify tools related to 'available expertise on infection management'. 'Accountability and responsibilities' tools were directed to both administrators and medical/nursing staff. We also found tools for 'monitoring and surveillance' and 'reporting and feedback', but in small numbers. Some ($n=17$) were not categorized, because they spanned the whole range of core elements (Table 2).

Further details on the identified tools can be found in Table S3.

Discussion

We conducted a systematic review of interventional studies evaluating AMS interventions in NHs, as well as guidelines/guidance, reviews and expert-opinion pieces related to this topic. In addition, we present an original inventory of AMS tools freely available on

the internet, specifically designed for the NH setting. Our objective was to provide for AMS teams a comprehensive menu of possible interventions and tools they could use, to help them start or adapt their AMS programmes in NHs.

Several reviews have been published recently on AMS in NHs,^{5,26–32} or are underway (<https://www.crd.york.ac.uk/PROSPERO/>) but we chose to use a different perspective. First, we included all types of interventional studies, to be as exhaustive as possible, while grading the level of evidence. Second, we categorized the interventions and tools according to recently published global AMS core elements, as the lack of uniformity in reporting data has been criticized.^{19,31} Finally, as this was not, to the best of our knowledge, available in the literature, we added an inventory of practical AMS tools, using a broad search strategy.

Wu *et al.*³³ recently published a meta-analysis including 11 interventional studies to evaluate the impact of AMS programmes in NHs and concluded that they reduce antimicrobial use by 14%. Even though the number of publications dealing with AMS in NHs is steadily increasing, the level of evidence is still insufficient and the design of interventional studies needs to be improved: only 5/18 interventional studies we found were randomized controlled trials and had a good-enough level of evidence based on the study design.^{22,34–37} Furthermore, sustainability and cost-effectiveness of the interventions are rarely addressed (Tables S1 and S2). Finally, it is important that future studies not only focus on antimicrobial consumption but also evaluate patient outcomes such as MDR-organism-related infections or colonizations, antibiotic-related adverse events and mortality.^{20,35,38–41} Guidance on the design and reporting of AMS interventions has been recently published and might be helpful.^{42,43}

Our results demonstrate the complexity of implementing an AMS programme in an NH setting. They also show that key elements of AMS apply to any setting.^{15,19,44,45} Among the AMS core elements, 'available expertise on infection management',

Table 1. Types of AMS intervention identified in the systematic literature review

AMS intervention category	Type of article		
	interventional studies	reviews and expert opinions	guidelines/guidance
Management leadership	—	Reviews: Crnich, ²⁸ Dyar, ²⁹ Morrill, ⁵ Katz ³⁰ Expert opinions: Martin, ^{63,64} Sloane, ⁶⁵ Jump, ⁶⁶ McElligott ⁶⁷	Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America (Barlam, 2016) ⁶⁸
Accountability and responsibilities	Decrease in overall antimicrobial use: Kasset ⁶⁰	Reviews: Fleming, ²⁶ Nicolle, ²⁷ Crnich, ²⁸ Dyar, ²⁹ Morrill ⁵ Expert opinions: Rhee, ⁶⁹ Martin, ^{63,64} Sloane, ⁶⁵ Jump, ⁶⁶ McElligott ⁶⁷	Core Elements of Antibiotic Stewardship for Nursing Homes (CDC, 2015) ¹⁵
Available expertise on infection management	Decrease in overall antimicrobial use: Jump ^{20a} Decrease in antimicrobial use for a specific indication: Doernberg ^{38a}	Reviews: Nicolle, ²⁷ Morrill, ⁵ Katz ³⁰ Expert opinions: Richards, ⁷⁰ Katz, ⁷¹ McElligott ⁶⁷	
Education and practical training	Improvement of guideline-adherent prescriptions: Naughton, ^{34a} Hutt, ^{39a} Monette, ^{37a} Schwartz, ^{40a} Linnebur ⁴¹ Decrease in overall antimicrobial use: Loeb, ³⁵ Zimmerman, ^{72a} Kasset ⁶⁰ Decrease in unnecessary antimicrobial use: Zabarsky, ^{62a} Trautner, ^{61a} McMaughan ⁷³ Decrease in a specific antimicrobial class: Pettersson ³⁶ Improved appropriateness of empirical antimicrobial prescriptions: Furuno ⁷⁴	Reviews: Fleming, ²⁶ Nicolle, ²⁷ Crnich, ²⁸ Dyar, ²⁹ Morrill, ⁵ Katz, ³⁰ Feldstein, ³¹ Falcone ³² Expert opinions: Moro, ⁷⁵ Rhee, ⁶⁹ Martin, ^{63,64} Sloane, ⁶⁵ Jump, ⁶⁶ McElligott ⁶⁷	
Other actions aiming at responsible antimicrobial use	Improvement of guideline-adherent prescriptions: Naughton, ^{34a} Hutt, ^{39a} Schwartz, ^{40a} Linnebur ⁴¹ Decrease in overall antimicrobial use: Loeb, ³⁵ Fleet, ^{22a} Zimmerman, ^{72a} Kasset ⁶⁰ Decrease in unnecessary antimicrobial use: Zabarsky, ^{62a} Rummukainen, ^{21a} Trautner, ^{61a} McMaughan ⁷³ Improved appropriateness of empirical antimicrobial prescriptions: Furuno ⁷⁴	Reviews: Fleming, ²⁶ Nicolle, ²⁷ Crnich, ²⁸ Dyar, ²⁹ Morrill, ⁵ Falcone ³² Expert opinions: Jump ⁶⁶	
Monitoring and surveillance	Decrease in overall antimicrobial use: Kasset ⁶⁰ Decrease in unnecessary antimicrobial use: Trautner ^{61a} Decrease in antimicrobial use for a specific indication: Doernberg ^{38a}	Reviews: Crnich, ²⁸ Dyar, ²⁹ Morrill, ⁵ Falcone ³² Expert opinions: Moro, ⁷⁵ Martin, ^{63,64} Sloane, ⁶⁵ Jump, ⁶⁶ McElligott ⁶⁷	
Reporting and feedback	Improvement of guideline-adherent prescriptions: Monette ^{37a} Decrease in overall antimicrobial use: Zimmerman, ^{72a} Kasset ⁶⁰ Decrease in unnecessary antimicrobial use: Zabarsky, ^{62a} Trautner ^{61a} Decrease in a specific antimicrobial class: Pettersson ³⁶	Reviews: Fleming, ²⁶ Nicolle, ²⁷ Crnich, ²⁸ Morrill ⁵ Expert opinions: Rhee, ⁶⁹ Martin, ^{63,64} Sloane, ⁶⁵ McElligott ⁶⁷	

A dash indicates that management leadership was not explored in any interventional studies included in this article.

^aStatistically significant impact of the intervention on the outcome.

‘educational and practical training’, ‘other actions aiming at responsible antimicrobial use’ and ‘reporting and feedback’ are the most promising interventions to implement in NHs (Table 1). This finding is consistent with recommendations from previously published reviews (Table S2). As found in the hospital setting, there

is no ‘one size fits all’ approach and the success of an AMS intervention likely depends on the context and the way the intervention is tailored to existing barriers and facilitators.⁴⁶

Regarding our inventory of tools, we noticed that many of them have been created recently, most likely driven by American

Table 2. Inventory of freely available tools for AMS programmes in NHs

AMS tool category	Number of relevant tools found
Management leadership	4
Accountability and responsibilities	7
Available expertise on infection management	0
Education and practical training	total: 58 professionals: 41 residents and families: 17
Other actions aiming at responsible antimicrobial use	total: 58 diagnosis/algorithms: 14 communication/assessment: 14 microbiology testing: 15 antibiograms: 15
Monitoring and surveillance	6
Reporting and feedback	6
General recommendations for implementation	17
Total	156

All tools are available in Table S3.

legislation, as most of them are from the USA.¹³ Most of these tools were created by regional or national health agencies and published on their website. Some agencies such as the CDC, the AHRQ or the Minnesota Health Department propose full programmes including most of the core elements and practical tools for implementing an AMS programme in an NH. The AHRQ website also adapts its offer based on the level of resources present in the NH.⁴⁷ The main interest of these tools is that they are specifically tailored for NHs and address the specificities of this setting. Because lack of funding and time are significant barriers to AMS implementation in NHs,⁵ we hope that the tools presented in our inventory will facilitate the work of AMS teams.

The importance of nurses for AMS in NHs is reflected in the number of interventions and tools (education, accountability and communication) targeted at them. They are often the only professionals available on site 24 h per day and physicians rely on their knowledge and experience to guide their antibiotic prescribing.⁴⁸ The 'assessment and communication' category provides tools for patient evaluation and reporting by the nurse to an off-site physician and may avoid unnecessary antibiotic prescriptions, as it was reported that out-of-hours doctors are more likely to prescribe antibiotics.⁴⁹

Education about AMR and the effectiveness of AMS is also a cornerstone in the implementation strategy, as reflected by the number of interventions and tools including an educational component. A recent survey reported that NH caregivers do not think that AMR is an issue in their practice and that there is a lack of awareness that antibiotic prescribing contributes to the public health problem of AMR.⁵⁰ We can assume that the motivation to participate in AMS activities would be higher if education were provided to NH health professionals. Residents' families should also receive some education on the topic, as they might expect antibiotics to be prescribed, according to physicians.⁴⁹

In 2016 in the USA, the reform of requirements for LTCFs by the centres for Medicaid and Medicare services were published and required 'facilities to develop an infection prevention and control program (IPCP) that includes an antibiotic stewardship program and designate at least one infection preventionist'.¹³ More specifically regarding AMS, they required NHs to 'include antibiotic use protocols and systems for monitoring antibiotic use' and 'record incidents identified under the facility's IPCP and the corrective actions taken by the facility'. To help NHs comply with these requirements, the CDC published core elements for antibiotic stewardship in NHs.¹⁵ As observed in our inventory of tools, many US state agencies created toolboxes to guide NHs in the implementation of AMS programmes. In Europe, the 2017 EU guidelines for the prudent use of antimicrobials in human health recommended that NHs 'ensure that antimicrobial stewardship activities are in place and are given dedicated time and management support' and should 'establish a multifaceted approach which includes elements such as education of nursing and medical staff, audits of antimicrobial use, feedback to the prescriber and targeting identified areas of antimicrobial overuse and misuse'.¹⁴ A list of national action plans and strategies to fight AMR in Europe is available, but only a few countries (e.g. Luxembourg, the Netherlands) explicitly mention measures targeting NHs (based on the review of the documents available in English).⁵¹

The implementation of AMS programmes can be seen as complex, especially in small care facilities like NHs. First, the AMR threat is often not perceived as a major issue, as demonstrated by previously cited surveys.^{49,50} The review published by Morrill *et al.*⁵ highlighted many barriers such as the paucity of well-validated strategies for NHs, the lack of funding and facility resources and the high prevalence of diagnostic uncertainty. Such difficulties are similarly found in small hospitals trying to implement AMS programmes, even though financial and management support is recommended in all facilities.⁵²⁻⁵⁴

A recent Cochrane review published in 2017 by Davey *et al.*⁵⁵ showed similar results in the hospital setting for AMS implementation. The number of high-quality randomized controlled studies was low and the majority of studies had a high risk of bias. Concerning the impact of these hospital-based interventions, the results were comparable to our NH findings regarding guideline-adherent prescriptions and antimicrobial use, but economic (length of stay) and microbiological (*C. difficile* infections and MDR organisms) outcomes have been explored in the hospital setting, whereas they are lacking in the NH setting.

Based on the definitions proposed by the 2013 ECDC point prevalence survey of healthcare-associated infections and antimicrobial use in European LTCFs, we can broadly differentiate three types of facilities for elderly people: (i) residential homes or assisted-living communities for people needing help with activities of daily living (ADL), (ii) general NHs or skilled-nursing facilities where patients are given help for ADL and need medical care with nursing staff available 24 h per day; and (iii) specialized LTCFs providing one specific type of care. This classification is consistent with information found on the NIH (USA), NHS (UK) and French Ministry of Health websites. It is important to note that terminology varies from one country to another.^{16,56-58} A survey published in 2017 and conducted in 17 countries (Australia, Canada, China, Czech Republic, England, France, Germany, Hong Kong, India, Italy,

Japan, Korea, Lebanon, the Netherlands, Scotland, Spain and the USA) demonstrated that the name 'nursing home' could encompass two to six types of different facility, from an assisted-living community to a geriatric hospital.⁵⁹ They proposed a definition for 'nursing home' as a facility that provides 24 h functional support for people who require assistance with ADL and have identified health needs. To deal with this terminology variation issue, we carefully double-checked the full text of each manuscript when in doubt regarding the type of care provided to elderly people. For example, two studies that are included in our systematic review were performed in hospital-based facilities for elderly people, including both NH care and acute care wards for elderly people, but we only included the results concerning NH residents.^{40,60} Moreover, four studies were conducted in State Veterans Homes, which is a unique system in the USA for disabled veterans, which can consist of NH care or adult day healthcare.^{20,39,61,62} Standardizing terminology and definitions at international level would certainly be most helpful.

The main strengths of our systematic literature review are the lack of language restriction, the large selected period (from inception to June 2018) and the selection and data extraction by two independent reviewers to ensure accuracy. The main limitations are the search being restricted to one database (MEDLINE) and the exclusion of grey literature sources. The main limitation of our website search for tools is the inclusion of websites mainly in English or French, so we might have missed tools available in other languages. This limitation is balanced by the international experts' survey we performed, which included experts from 21 different countries. Finally, although the tools we included in our inventory are tailored to the NH setting, we could not find any reports or studies evaluating these tools. It would be interesting to have 'real-life' evaluations to support the use of these tools.

In conclusion, our work offers AMS experts a wide range of interventions and tools they might use to implement AMS programmes in NHs. High-quality interventional studies are needed to further assess the impact of AMS interventions on antimicrobial use in NHs and should explore microbiological (resistance data), patient (adverse events, hospital admission, mortality) and economical outcomes.

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Transparency declarations

None to declare.

Supplementary data

Tables S1 to S3 are available as [Supplementary data](#) at JAC Online

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ARTICLE 2 : ANTIBIOTIC STEWARDSHIP IN FRENCH NURSING HOMES : A READINESS ASSESSMENT SURVEY

Antibiotic stewardship in French nursing homes: a readiness assessment survey

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Introduction

In Europe, in 2015, antibiotic resistance was responsible for about 33 000 deaths and costed about 1.1 billion euros to the healthcare system of EU/EEA countries ¹. The two major drivers for antibiotic resistance are the use of antibiotics which exert an ecological pressure on bacteria and contribute to emergence and selection of antibiotic-resistant bacteria in the population, as well as spread and cross transmission of resistant micro-organisms ².

To tackle the global antibiotic resistance threat, antibiotic stewardship (ABS), which is defined as “a coherent set of actions designed to use antibiotics responsibly” has been advocated since the late 1990s ³. Primarily studied in the hospital setting, it has been shown that multidrug-resistant bacterial infections or colonizations can be reduced by the implementation of antibiotic stewardship programs ⁴. Nursing homes (NH), which are defined as facilities that provide 24/7 functional support for people who require assistance with activity of daily living and have identified health needs, also have antibiotic use and resistance issues ^{5,6}. The 2016 European point prevalence survey of healthcare-associated infections and antimicrobial use showed that 4.9% of long term care facilities residents were receiving antibiotics on the day of the survey with large variations between countries (from 0.7% to 10.5%), including about one third of prescriptions for prophylaxis ⁷. In the US, the CDC found that up to 70% of nursing home residents received antibiotics each year and that 40-75% of prescribed antibiotics were inappropriate or unnecessary ⁸. Moreover, living in a high antibiotic use NH (as compared to a low-use one) was associated with a 24% increased risk of experiencing any antibiotic-related adverse event (including *Clostridioides difficile* infections, infections with antibiotic-resistant bacteria or general adverse events) ⁹. Several interventional studies or reviews investigating ABS programmes in NH have been published

recently^{10–18}, and a meta-analysis of these studies concluded that ABS implementation in NH can reduce antibiotic use by 14%¹⁹. In the US, the CDC has developed core elements of ABS programmes that are specifically adapted to the NH context⁸.

Less than ten questionnaire surveys have assessed to what extent ABS programmes are implemented in NH^{7,20–25}. More than half of them were conducted in the US, where ABS programmes have been mandatory in NHs since 2016, with only one of these surveys having been performed in the last four years²³. In Europe, two surveys were conducted in Ireland and Belgium, with the 2016 ECDC HALT point-prevalence survey also providing some information on ABS activities in 1 788 NHs in 26 European countries. No data are available for France on this topic to the best of our knowledge.

Our objective was to describe antibiotic stewardship current practices as well as opportunities for improvement in nursing homes in one French region, using a questionnaire survey.

Methods

Nursing homes (NHs) context in France

In France, NH residents are usually aged 65 or older and may stay temporarily, but more frequently permanently in the NH. They need constant supervision and nursing care, but they are medically stable and do not need invasive medical procedures or constant medical care. Residents are free to choose their own general practitioner (GP), who is not an employee of the NH present on-site and is frequently the same GP they had while living in the community. Some NHs are hospital-based NHs (18.8% in France) and then benefit from the hospital transversal services such as on-site pharmacy, laboratory or imaging facility; in that case, their ABS activities are those of the hospital they are related to. However, most French NHs are community-based NHs and then do not have on-site pharmacy or biology/imaging services; in these NHs, residents can also choose their community pharmacy, biology or radiology provider. These NHs do not have any mandatory requirement to implement ABS programmes.

Design of the questionnaire

We first performed a literature review of published surveys about antibiotic stewardship programmes in NH²⁰⁻²⁹, as well as core elements of NH antibiotic stewardship programmes^{8,18}. The draft questionnaire was then reviewed by the scientific committee composed of infectious diseases specialists, public health specialists, general practitioners (taking care of NH residents) and representatives of several regional health authorities or organizations that officially supported the survey (Agence régionale de santé Grand Est ; AntibioEst ; Direction régionale du service médical Grand Est ; Observatoire des médicaments, dispositifs médicaux et innovations thérapeutiques Grand Est). The questionnaire was validated during a scientific committee meeting and pilot-tested by ten NH medical coordinators.

The final questionnaire (available as a supplementary file) included 35 questions covering four main topics: nursing home characteristics, current antibiotic stewardship practices (including core elements of NH antibiotic stewardship programmes) and suggestions for improvement. Some items were evaluated using a 5-point Likert scale, ranging from 0 (no interest/impact) to 5 (maximal interest/impact).

Sample selection

The study population included all community-based nursing homes in the region Grand Est in northeastern France (5 555 186 millions inhabitants in 2016) ³⁰.

Survey administration

AntibioEst (the regional antibiotic stewardship network, that has been in place since 2003) sent an e-mail to all eligible NHs, including an invitation letter (mentioning all organizations supporting the survey), a weblink to the online survey (available on SurveyMonkey®) and a PDF version of the questionnaire. A joint reply by both the medical and nurse coordinators was recommended. Each facility could either reply to the survey online or send the completed PDF by e-mail or postal mail.

The survey opened on 4th June 2019 and was closed on 30th November 2019. Up to three reminders were sent to NHs. Non-responding NHs were also contacted by phone after the second reminder. They were asked if they had received the e-mail invitation and encouraged to participate in the survey; their contact details were also double checked. No incentives were provided, except feedback on the results of the survey.

Data analysis

Data were anonymized for the analysis. The descriptive analysis of the results was performed using Excel®.

Ethical statement

This study did not modify the medical care of residents, and anonymity was preserved during the analyses. An ethical committee was therefore not required, according to the French law.

Results

Characteristics of participating nursing homes (Table 1)

Out of 417 community-based NHs, 75 (18%) participated in our survey. The medical coordinator replied on his/her own in more than half of the cases (38/71, 53%), with 23% (16/71) of joint replies by the medical and nurse coordinators.

Almost all responding facilities had a nurse coordinator (70/72, 97%) and/or a medical coordinator (63/72, 88%). The median number of general practitioners who took care of at least one resident in each nursing home was 15, ranging from 3 to 52. The median full-time equivalents working in nursing homes was 0.4 for medical doctors, 4 for nurses and 18 for nurse assistants. Forty percent of facilities were part of a manager group of nursing homes, and most facilities had a partnership with a community pharmacy (83%) or a biology laboratory (82%). All but one nursing home had computerized medical records and 73% computerized antibiotic prescribing.

Current antibiotic stewardship practices

Standard elements of antibiotic stewardship programmes were overall usually present in less than half of participating NHs (Table 2).

Only 22% (16/72) had a professional responsible for coordinating infection/antibiotic management activities in the NH. His/her roles were to help manage infection treatment (12/16), to promote antibiotic stewardship (10/16), to help with infection diagnosis (8/16) and/or to monitor antibiotic resistance (4/16) in the facility. Half of these professionals were the medical coordinator of the facility and in some cases (4/16), a nurse was responsible.

More than half (38/71, 54%) of the responding facilities proposed a therapeutic guide for antibiotic prescribing for common infections (urinary, respiratory or skin infections) but guides dealing with the diagnostic process were less frequently available. Only 28% of NHs informed prescribers about ANTIBIOTEL, a regional service where an infectious diseases specialist is available on the phone for advice for free.

Recording indication, dosing and duration when antibiotics were started was requested in more than half of the facilities but in 60% of NHs, there was no systematic reassessment of treatment at 48-72 hours or at 7 days. Educational sessions about infection management and/or antibiotic prescribing had been offered in the past 3 years for nursing staff and medical staff in respectively 23% and 29% of the responding facilities, but only few (9/70, 13%) organized internal audit to evaluate practices on antibiotic use and/or infection management. About 2/3 of nursing homes had access to their antibiotic use data (at least annually) but only 1/3 had access to bacteriological data. Some respondents reported other ongoing initiatives in a free-text box, such as antibiotic stewardship discussions at the regional geriatric committee and frequent communication between physicians and the nursing staff.

Suggestions for improvement (Table 3)

Overall, most suggestions were perceived as useful by the participants, except the ones related to the involvement of residents or their relatives as well as administrative directors.

The interventions that were perceived as being the most useful were educational sessions for physicians, the distribution of antibiotic prescription guides and documenting an antibiotic plan.

Discussion

Our results show that antibiotic stewardship programmes are insufficiently implemented in French nursing homes, even though the medical and nurse coordinators who participated in our survey seemed aware this is a public health priority. Most propositions were favorably welcomed when asking about antibiotic stewardship opportunities and several suggestions for improvement were made by the participants including education of physicians related to antimicrobial resistance, financial and staff support.

Overall, out of the 72 facilities, only 2 nursing homes did not have any antibiotic stewardship activity (3%). In a recent Belgian survey, only 23% of 39 facilities had an ASP²⁷. This is consistent with the results of a survey in Michigan in 2014 in which 75% of responding facilities reported having antimicrobial stewardship policies or procedures but only 23% having a formal ASP with dedicated staff²².

We summarized the results of implemented antibiotic stewardship strategies in nursing homes in our region and compared it to our literature review of previous surveys (Table 4). The ABS categories most frequently implemented in both our survey and the literature were monitoring of antibiotic use, availability of guidelines for appropriate antibiotic use, documentation of the antibiotic plan and reassessment of prescribed antibiotics. These strategies were also the most positively perceived by our survey respondents, probably because they are easy to implement and they are not time or money consuming. Conversely, available expertise on infection management and education strategies were less frequently observed in our study as compared to previously published surveys. It is quite surprising as ID specialists are freely available on the phone in our region and education was positively perceived. Because lack of awareness of prescribing guidelines and impact of antimicrobial overuse on antimicrobial resistance are known barriers to ABS implementation^{31,32}, education-based interventions should be implemented to increase knowledge and motivation to participate in antimicrobial stewardship activities and should target both NH caregivers, residents and their relatives.

We did not assess management leadership and financial support in our survey, as ABS is currently not a mandatory requirement in French NHs, but these items had low implementation rate in the published literature ²¹.

A recent survey tried to determine factors that were associated with low rates of antibiotic use in nursing homes and they found that facilities where education, feedback and comparison of antimicrobial use with other facilities, or with a local leader for infection prevention and control had lower rates of antibiotic use ³³. This was confirmed by Fu *et al.* who showed that the presence of a certified infection prevention and control leader was associated with more comprehensive antimicrobial stewardship programmes, as well as an occupancy rate >75%, being part of a for-profit group of nursing homes or participating in a health quality programme ²³. Being better prepared for IPC might facilitate implementation of ABS activities. Many reviews about antimicrobial stewardship in nursing homes have emphasized the importance of having a local leader within the facility to lead implementation ^{13,15,17}. In our survey, only 22% of responding nursing homes had an identified professional in charge for infection/antibiotic management. If we could increase this number, it would probably help many facilities to start an ABS programme.

Our study brings original findings, but it has some limitations. The response rate was quite low (21%), despite several reminders, as in several other published surveys ^{23–25,27}. It is possible that the most advanced or motivated NHs replied to our questionnaire, meaning that our results might present an optimistic perspective on the true ABS situation in our region. We also could not collect information about non-responding facilities' characteristics, to assess if respondents were representative of all NHs in our region. However, when comparing the FTE for medical and nurse coordinators to a 2015 national survey, similar results were found ³⁴. Finally, although we asked both medical and nurse coordinators to reply jointly to the questionnaire, this was the case in less than a quarter of cases, which may limit the validity of some replies.

In conclusion, French nursing homes have started to implement strategies to improve antibiotic use, with NHs' stakeholders having a favorable attitude towards ABS, but there is still room for improvement. Defining ABS core elements for NHs at national level would be helpful. Regional health authorities, with the support of regional antibiotic stewardship networks, could then take a leading role in implementing these elements. The inventory of practical tools we published recently might be a starting point to stimulate sharing of best practices¹⁸.

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Tables

Table 1. Characteristics of participating nursing homes (NHs), Grand Est region, northeastern France, 2019

Characteristics	Respondents (n/N)	Responses
Facilities with (%) :		
- Medical coordinator	63/72	88
- Nurse coordinator	70/72	97
Mean full-time equivalents (median [IQR]) :		
- Medical coordinator	66	0.4 [0.3-0.5]
- Nurses	69	4 [3.5-5]
- Nurse assistants	63	18 [14-21]
Mean number of GPs taking care of NH residents (median [IQR]) :	67	15 [8.5-22.5]
Partnership with (%) :		
- Local/regional hospital	9/72	12
- Community pharmacy	60/72	83
- Biology laboratory	59/72	82
Facilities part of a manager group (%)	29/72	40
Computerized medical records (%) :		
- Yes, for all data	55/71	78
- Yes, for some data	15/71	21
- No	1/71	1
Computerized medication prescribing (%) :		
- Yes, for all drug prescriptions	50/71	70
- Yes, for some	16/71	23
- No	5/71	7
Computerized antibiotic prescribing (%) :		
- Yes, for all antibiotic prescriptions	52/71	73
- Yes, for some	12/71	17
- No	7/71	10
Professionals responding to the survey (%) :		
- Medical coordinator	38/71	53
- Nurse coordinator	13/71	18
- Both	16/71	23
- Other	4/71	6

GP : general practitioner ; IQR : interquartile range

Table 2. Current antibiotic stewardship strategies implemented in participating nursing homes

Strategy	Respondents n/N	Responses (%)
Identification of a NH professional responsible for coordinating infection/antibiotic management activities in the NH	16/72	22
Written protocols for the infection diagnosis process :		
- For physicians	12/71	17
- For nurses	27/71	38
- None	44/71	60
Written protocols to guide the indication / sampling / interpretation / therapeutic management for :		
- Urinary dipsticks	29/68-33/67- 25/64-11-64	43-49-39- 17
- Urine cultures	39/70-47/69- 21/65-14/66	56-68-32- 21
- Blood cultures	17/66-20/63- 8/61-6/61	26-32-13- 10
Therapeutic guide (paper or electronic) for antibiotic prescribing for common infections	38/71	54
Prescribers being informed about the regional ANTIBIOTEL service (infectious diseases specialist available on the phone for advice for free)	16/71	23
NH policy recommending documenting the antibiotic plan at initiation in the medical record (indication, dosing and duration)	39/70	56
NH policy recommending systematic reassessment of each antibiotic treatment :		
- Yes, at 48-72 hours	24/71	34
- Yes, at 7 days	9/71	13
- None	42/71	59
NHs having organized training sessions about infection management and/or antibiotic prescribing in the past 3 years :		
- Yes, for medical staff	16/70	23
- Yes, for nursing staff	20/70	29
- None	45/70	64
NHs having organized internal audits on antibiotic use and/or infection management in the past 3 years	9/70	13
NHs having access to their antibiotic use data (at least annually)	47/72	65
NHs having access to their bacteriological data (at least annually)	26/72	36

NH : nursing home

Table 3. Perceptions and suggestions for improvement regarding antibiotic stewardship in nursing homes

Affirmation	Respondents (n)	Mean score
Antibiotic stewardship is of major public health importance	52	4.6
I wish antibiotic stewardship would become a priority objective in my facility in the coming years	54	4.2
The following persons could influence antibiotic prescribing in my facility :		
- Residents	52	1.4
- Residents' relatives	53	2
- Medical coordinator	54	4.3
- Nurse coordinator	53	3.6
- Residents' GPs	54	4.6
- Other prescribers (dentists, other specialists)	54	3.4
- Nursing staff	53	3.4
- Administrative director	53	1.5
- Biologists	52	2.6
- Community pharmacists	53	2.7
An antibiotic stewardship commitment poster displayed in my facility	51	2.8
Educational sessions about antibiotic stewardship targeting :		
- Residents' GPs	53	4.2
- Nurses	53	3.8
- Nurse assistants	53	2.2
- Residents	52	1.7
- Residents' relatives	52	2
- Medical coordinator	53	4
- Nurse coordinator	53	3.8
Educational sessions about microbiology testing focusing on :		
- Indication	54	3.8
- Sampling	54	3.5
- Interpretation	54	3.8
Antibiotic prescription guides distribution	53	4.2
Documentation of an antibiotic plan (indication, dosing and duration) in the patient record	52	4.1
Design of indicators assessing the appropriateness of antibiotic prescriptions	54	3.8
Design of indicators assessing the appropriateness of microbiological tests	53	3.8
Audit implementation	54	3.4
Feedback about quantity of antibiotic use in the NH to medical and nursing staff with comparison to other facilities	54	3.4
Feedback about resistance data of the NH to medical and nursing staff with comparison to other facilities	52	3.5

Each item was rated on a 5-point Likert scale from 0 (totally disagree, minimum interest/impact) to 5 (totally agree, maximum interest/impact) ; GP : general practitioner ; NH : nursing home

Table 4. Presence of antibiotic stewardship core elements in our study as compared to previously published surveys.

AMS core elements	Our results	Literature review results
Management leadership		<ul style="list-style-type: none"> - Formal written support from leadership : 28% (Morrill²¹) - Financial support for AMS : 15% (Morrill²¹)
Accountability & responsibilities	<ul style="list-style-type: none"> - Identification of a NH professional responsible for coordinating infection/antibiotic management activities in the NH : 22% 	<ul style="list-style-type: none"> - Formal ASP policies : 23% (Malani²²), 59.5% (Van Schooneveld²⁴) - AMS committee : 16% (Donlon²⁰)
Available expertise on infection management	<ul style="list-style-type: none"> - Infectious diseases specialists counseling : 23% 	<ul style="list-style-type: none"> - Infectious diseases specialists counseling : 54% (Morrill²¹) - Pharmacists guidance or expertise on antibiotic use : 89% (Morrill²¹)
Education & practical training	<ul style="list-style-type: none"> - Education and practical training : <ul style="list-style-type: none"> - designed for physicians : 23% - designed for nursing staff : 29% 	<ul style="list-style-type: none"> - Education and practical training : 63.2% (Fu²³), 56.8% (Van Schooneveld²⁴), 35.5% (Yang²⁵), 20.7% (HALT-3⁷) <ul style="list-style-type: none"> - designed for physicians : 7% (Donlon²⁰), 90% (Morrill²¹), 7.1% (Van Schooneveld²⁴) - designed for nursing staff : 78% (Morrill²¹) - designed for residents and family : 71% (Morrill²¹)
Other actions aiming at responsible antimicrobial use	<ul style="list-style-type: none"> - Guidelines for appropriate use : 54% - Antibiotic plan and reassessment : 56% - 34% (48-72h) ; 13% (day7) - Written protocols for infection diagnosis designed for physicians : 17% ; and designed for nursing staff : 38% 	<ul style="list-style-type: none"> - Guidelines for appropriate use : 28% (Donlon²⁰), 79.8% (Yang²⁵), 39.4% (HALT-3⁷) - Antibiotic plan and reassessment : 45%-38% (Morrill²¹) - Therapeutic formulary : 23% (Donlon²⁰), 65.7% (Fu²³), 36% (Malani²²), 19.4% (Morrill²¹), 27.4% (Yang²⁵) - Pre-approval form : 12% (Donlon²⁰), 10.8% (Van Schooneveld²⁴), 25% (Yang²⁵) - List of restricted antibiotics : 19% (Fu²³), 24% (HALT-3⁷) - Antimicrobial de-escalation : 49% (Fu²³)

Monitoring & surveillance	<ul style="list-style-type: none"> - Antibiotic use : 65% - Resistance data : 36% 	<ul style="list-style-type: none"> - Antimicrobial use : 16% (Donlon²⁰), 91.4% (Fu²³), 52% (Malani²²), 92% (Morrill²¹), 81% (Van Schooneveld²⁴), 81.5% (Yang²⁵) - Resistance data : 12% (Donlon²⁰), 58% (Malani²²), 89% (Morrill²¹), 76% (Van Schooneveld²⁴) - Individual prescribers antimicrobial use : 10.8% (Van Schooneveld²⁴) - Antimicrobial costs : 32.4% (Van Schooneveld²⁴)
Reporting & feedback		<ul style="list-style-type: none"> - Antimicrobial data : 10% (Donlon²⁰), 68.9% (Fu²³), 75% (Morrill²¹) - Clinical cases review : 80.7% (Fu²³), 90% (Malani²²), 81.1% (Van Schooneveld²⁴)

AMS : antimicrobial stewardship ; ASP : antimicrobial stewardship programme ; NH : nursing home

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CONCLUSION

Nous avons montré d'une part que des études interventionnelles de niveau de preuve variable ont pu mettre en évidence un effet des stratégies de bon usage des antibiotiques lorsque celles-ci sont appliquées aux EHPAD, notamment sur l'amélioration des prescriptions selon les recommandations, la diminution de la consommation totale d'antibiotiques et sur la diminution des prescriptions d'antibiotiques jugées inutiles (comme pour les bactériuries asymptomatiques). Nous avons également identifié les interventions qui ont montré les effets les plus importants, à savoir les stratégies d'éducation, les stratégies de surveillance et de feedback associé ainsi que l'expertise de spécialistes en maladies infectieuses. Nous avons listé de nombreux outils disponibles gratuitement sur internet pour aider au développement de la mise en place de programmes de bon usage des antibiotiques au sein des EHPAD. Nous avons d'autre part, via l'enquête régionale réalisée, pu montrer que des initiatives locales existaient déjà et que l'accueil des propositions concernant la mise en place de stratégies de bon usage des antibiotiques est plutôt positif. Ceci s'explique sans doute par une prise de conscience de la problématique de l'antibiorésistance et à une volonté d'améliorer les pratiques dans ce domaine.

Il est avant tout nécessaire de produire des études interventionnelles de haut niveau de preuve. En effet, une méta-analyse publiée en 2020 par Raban *et al.* n'a pu mettre en évidence d'effet des différentes interventions pour réduire la consommation totale d'antibiotiques, améliorer la pertinence des prescriptions d'antibiotiques ou la pertinence du choix de l'antibiothérapie probabiliste en EHPAD du fait du faible nombre d'études incluses et du risque de biais important dans ces études [32]. Nous avons déjà soulevé ce point dans notre revue de littérature puisque parmi les 18 études interventionnelles incluses, seulement 5 étaient des études randomisées contrôlées [33]. Afin d'améliorer la comparabilité des études, il est nécessaire d'harmoniser les méthodologies de recherche en se basant par exemple sur les éléments clés des programmes de bon usage des antibiotiques publiés en 2018 par Pulcini *et al.* que nous avons utilisés pour notre revue de littérature afin de définir les interventions les plus efficaces [34]. Il est également nécessaire d'utiliser des critères de jugement cliniques (mortalité, colonisation ou infection à BMR) et économiques plutôt que des critères intermédiaires comme le respect des recommandations ou la

consommation totale d'antibiotiques. Des essais randomisés contrôlés étudiant des critères d'évaluation cliniques permettraient d'obtenir un meilleur niveau de preuve pour rédiger des recommandations sur la mise en place de programmes de bon usage des antibiotiques dans les EHPAD. Cependant, même en l'absence de recommandations formelles, compte tenu de la forte consommation d'antibiotiques, souvent inappropriée, et connaissant ses conséquences, il est important d'ores et déjà de mettre en place des programmes de bon usage des antibiotiques dans les EHPAD, en se basant sur la littérature existante.

Pour que ces programmes de bon usage puissent être implantés rapidement et de manière durable, il est important de pouvoir accompagner les EHPAD dans la mise en place de ces programmes. La liste des outils que nous avons pu fournir dans notre revue de littérature peut servir de base pour l'initiation de tels programmes, en procédant par étapes [33]. L'identification d'un personnel ou d'un comité responsable de la coordination de ces programmes au sein de l'établissement permettrait de donner l'impulsion et d'assurer la motivation pour poursuivre les efforts. Bien sûr, les nombreuses problématiques des EHPAD relatives à la polypathologie, la polymédication, la dépendance des résidents ainsi que les problèmes de recrutement et de turn-over des personnels ne facilitent pas le démarrage de telles initiatives, qui nécessitent des moyens humains et financiers conséquents. Selon l'enquête Prév'EHPAD de 2016, seulement 45,3% des établissements avaient accès à un référent en antibiothérapie et 59,4% avaient un référent en hygiène présent sur le site [27]. Il sera donc nécessaire à l'avenir de pouvoir apporter une expertise 'hors les murs' aux établissements qui le souhaitent, avec un soutien de spécialistes en gériatrie, en maladies infectieuses, en hygiène et prévention/contrôle des infections, et en santé publique pour aider à mettre en place ces programmes de bon usage des antibiotiques.

L'objectif de lutte contre l'antibiorésistance doit également être associé à des politiques de vaccination et de prévention/contrôle des infections, communautaires comme associées aux soins. Une enquête française de 2011 sur la vaccination antigrippale et antipneumococcique dans 175 EHPAD notait une couverture vaccinale de 80,8% pour la grippe et de 28% pour le pneumocoque [35]. Des résultats similaires étaient mis en évidence pour la grippe aux États-Unis pour la période 2014-2015 (couverture vaccinale de 75,7% des résidents) mais avec une meilleure couverture vaccinale pour le pneumocoque (80%) [36].

La problématique de la vaccination antigrippale est encore plus marquée chez les professionnels de santé exerçant dans les EHPAD puisqu'une enquête menée dans le département de l'Ille-et-Vilaine avait mis en évidence une couverture vaccinale de seulement 20% du personnel interrogé (477 employés) pour la saison 2015-2016, chiffre bien inférieur au seuil de 75% fixé par le ministère de la santé pour le personnel travaillant au sein d'EHPAD [37]. Un âge supérieur à 30 ans, un antécédent de grippe « sévère » ou le fait de travailler en tant que professionnel de santé au sein de l'établissement (en comparaison avec les personnels de maintenance et logistique) ont été identifiés comme des facteurs favorisant la vaccination antigrippale dans cette étude. Dans l'enquête de prévalence des infections associées aux soins Prév'EHPAD 2016, la prévalence de ces infections était de 3,0% et les caractéristiques des EHPAD ayant une prévalence plus élevée comprenaient notamment le nonaccès à une expertise en hygiène et l'absence de correspondant en hygiène, facteurs qui n'étaient pas retrouvés en analyse multivariée [27]. Cependant, l'absence d'un correspondant en hygiène était associée en analyse multivariée à une prévalence plus élevée de prescription d'antibiothérapie (RR = 1,3).

Enfin, sur le modèle de ce qui a été fait aux États-Unis dans le cadre du programme *Medicare and Medicaid*, imposant depuis 2016 à tous les établissements de soins de longue durée (« long term care facilities »), ce qui correspond pour partie aux EHPAD en France, il serait important de rendre obligatoire la présence de programmes de bon usage des antibiotiques dans les EHPAD français. Au niveau européen, le centre européen de prévention et de contrôle des maladies recommande, dans ses propositions pour le bon usage des antibiotiques en médecine humaine, l'instauration de programmes de bon usage des antibiotiques dans les EHPAD avec du temps et des moyens dédiés incluant notamment des actions d'éducation du personnel médical et paramédical, d'audit et de feedback ; seulement 2 pays (Pays-Bas et Luxembourg) incluaient cependant ces actions dans les EHPAD dans leur plan d'action national Antibiorésistance [38,39]. La Feuille de route française 2016 pour la maîtrise de l'antibiorésistance intégrait des actions de promotion de bon usage des antibiotiques en EHPAD, mais seule une partie des actions a été mise en place à ce jour. Il est donc urgent de renforcer ces actions au niveau local, régional et national.

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APPENDIX A – DETAILED INFORMATION ON THE 18 INCLUDED INTERVENTIONAL STUDIES

Study	Objective	Setting/Period of time/Design	Intervention	Outcomes	Level of evidence ^a
Naughton et al. (2001) ¹	To evaluate the effect of implementation of nursing home-acquired pneumonia guidelines on antibiotic use, hospital admission and mortality	<u>Setting:</u> 10 skilled nursing facilities (USA) <u>Period:</u> Pre-intervention 6 months , post intervention 6 months <u>Design:</u> Randomized controlled study	Multifaceted intervention: Education: Small group discussion + laminated cards (Physician only intervention group) vs small group discussion + 1h training session for nurses + laminated cards + posters (multidisciplinary intervention group) Other actions: Guidelines	Pre/post intervention guideline adherence: - Intravenous prescriptions : 62.2% vs 73.4% (p=0.15) - More IV use in accordance with guidelines post intervention (p<0.02) (multivariate analysis) - No difference between multidisciplinary vs physician only group Pre/post intervention oral prescriptions in accordance with guidelines: no difference (p=0.27) No significant difference in hospitalization rate or 30-day mortality	Good
Loeb et al. (2005) ²	To assess whether a multifaceted intervention can reduce the number of prescription of antimicrobials for suspected UTI in NH residents	<u>Setting:</u> 20 NHS (Canada/USA) <u>Period:</u> 1-year follow-up post intervention <u>Design:</u> Cluster randomized controlled study	Multifaceted intervention: Education: 30 min. case scenarii for nurses, one-to-one interview for prescribers, pocket cards and posters Other actions: Diagnostic algorithms	Number of antimicrobial prescriptions (per 1000 resident days): no significant difference (3.52 courses in Intervention Group vs 3.93 in Control Group ; weighted mean difference -0.37; IC -1.17 to 0.44) Rate of antimicrobial use for suspected UTI (per 1000 resident days): 1.17 courses in IG vs 1.59 in CG (weighted mean difference -0.49; 95CI -0.93 to -0.06): reduction persisted overtime but not significant Hospital admissions (per 1000 resident days): no difference (0.98 for IG vs 0.81 for CG) Mortality (per 1000 resident days): no difference (1.11 in IG vs 1.09 in CG)	Good
Hutt et al. (2006) ³	To assess the effect of a multifaceted intervention on nursing home-acquired pneumonia management	<u>Setting:</u> 2 State Veterans Homes (USA) <u>Period:</u> baseline: 1 year ; post intervention: 1 year <u>Design:</u> controlled before-after study	Multifaceted intervention: Education: educational session for nursing staff about guidelines + booklet, pocket cards and posters; academic detailing for physicians Other actions: Diagnosis/communication (pre-printed form)	Improvement of guideline adherence after the intervention: - Appropriate antibiotic use 81% IG vs 33% in CG (p<0.05) - Timely antibiotic prescriptions 79% in IG vs 17% in CG (p<0.05) Improvement in the intervention group pre/post intervention: - Influenza vaccine +24% (p<0.05) - Timely physician response +31% (p<0.05) - Chest X-ray + 49% (p<0.05) No significant difference in hospitalization rate or mortality	Fair

Monette et al. (2007) ⁴	To assess the effect of an educational intervention on optimization of antimicrobial prescribing in LTCF	Setting: 8 LTCFs (Canada) Period: 15 months (pre-intervention, post-intervention I, post-intervention II and follow-up) Design: pair-matched cluster randomized controlled trial	Multifaceted intervention: - Education: e-mailed guidelines - Feedback & reporting: e-mailed - prescribing profile with adherence to guidelines Conducted 3 times (at the beginning + every 4 months)	Non-adherent antibiotic prescriptions: -20,5% in IG vs -5.1% CG from baseline to follow-up Likelihood ratio of non-adherent antibiotic prescriptions between intervention and control group: significant difference in post intervention II period (OR 0.36 95CI 0.18-0.73) for the intervention group ; lower ratio for IG in post intervention I and follow-up but not statistically significant	Good
Schwartz et al. (2007) ⁵	To improve antimicrobial use in a hospital based LTCF using a multifaceted intervention	Setting: 1 hospital-based LTCF (USA) Period: pre-intervention period: 10 months ; intervention : 18 months ; post intervention period: 24 months Design: Before-after uncontrolled study	Multifaceted intervention: Education: 4 educational meetings for medical providers + presentation to nursing leadership + booklets Other actions: booklets including guidelines and algorithms	Guideline-adherent antimicrobial regimen: increased in post intervention vs pre (39% vs 11%; p<0.001) Mean monthly antimicrobial days: decrease of 29.7% (p<0.001) during the intervention period ; sustained for the 2 years follow up but not statistically significant Initiation of antimicrobials: -25.9% during intervention period but not significant (p=0.06) Overall and infection-related mortality: no difference	Fair
Zabarsky et al. (2008) ⁶	To assess the effect of a multifaceted intervention on asymptomatic bacteriuria overtreatment	Setting: 1 Veteran Affairs LTCF (USA); Period: 3 months pre-intervention and 30 months follow up Design: Before-after uncontrolled study	Multifaceted intervention: Education: educational meetings about guidelines for nursing staff and medical providers + pocket cards + posters + follow-up educational meetings bi-annually Other actions: pocket cards with criteria for diagnosis of symptomatic UTI Feedback: urine cultures sent and ASB treatment	ASB treatment: significant decrease from 68% in the pre-intervention to 44% in the post intervention period (p=0.022) Total antimicrobial days of therapy (per 1000 patient days): significant decrease from 167.7 to 117.4 in initial period (p< 0.001) to 109 in the continuing period (p<0.001)	Poor
Linnebur et al. (2011) ⁷	To assess the impact of a multidisciplinary intervention implementing guidelines for nursing home-acquired pneumonia	Setting: 16 NHs (USA); Period: Baseline 7 months and post intervention 2 x 7 months Design: Before-After controlled study	Multifaceted intervention: Education: interactive educational session for nursing staff + academic detailing directed to physicians + pocket cards + reprints of the guidelines Other actions: Communication/Diagnosis: Preprinted orders	Use of guideline-recommended antibiotics: no significant increase from 60% to 66% in the IG and 32% to 39% in the CG (p=0.3) Adherence to guideline recommending delivery of an antibiotic within 4h: increased from 57% at baseline to 75% at year 2 in IG, vs from 38% to 31% in CG (p=0.0003) Adherence to treatment duration: decreased in both IG (27% to 13%) and CG (24% to 19%) No difference in overall mortality	Fair

Pettersson et al. (2011) ⁸	To assess the effect of a multifaceted educational intervention on antibiotic prescribing in NHs	Setting: 46 NHs (Sweden) Period: Baseline 3 months , Intervention 4 months and Post intervention data collection 4 months Design: Cluster randomized controlled study	Multifaceted intervention: Education: focus group discussions with physicians, nurses and nurse assistants about guidelines and barriers + leaflets and handouts Feedback & reporting: baseline results and verbal summary at the end of the sessions	Proportion of quinolones for lower UTIs in women: significant decrease in both intervention (-0.196; CI95% -0.338, -0.054) and control group (-0.224, CI95% -0.394, -0.054) without significant difference between the 2 groups (0.028, CI95% -0.193, 0.249) Proportion of infections treated by antibiotics: significant decrease in IG vs CG (-0.124, CI95% -0.228, -0.019) Proportion of infection handled as “wait and see”: significant increase in intervention group vs control (0.143, CI95% 0.047, 0.240) No hospital admission increase in the intervention group	Good
Jump et al. (2012) ⁹	To assess the impact of an on-site LTCF infectious disease consultation on antimicrobial use and <i>Clostridium difficile</i> tests	Setting: 1 Veteran Affairs NH (USA) Period: Before: 36 months ; after: 18 months Design: Before-After uncontrolled study	Available expertise on infection management: Implementation of an infectious disease consultation team (1 ID physician and 1 nurse practitioner) for consults and on-call advice	Reduction of total antibiotic use post intervention in LTCF: 30.1% (p<0.001) Decrease in fluoroquinolones use post-intervention in LTCF: 38% (p<0.001) Decrease in sulfamethoxazole/trimethoprim use : 38% (p<0.001) Decrease in use of beta-lactam/beta-lactamase inhibitor use : 28% (p=0.0005) <i>Clostridium difficile</i> positive tests (per 1000 days of care): not significant -0.2 (CI95% -0.79, 0.28) but change in slope (interrupted time series analysis) statistically significant change: 0.1 (CI95% 0.0, 0.1)	Poor
Rummukainen et al. (2012) ¹⁰	To assess the impact of drawing local guidelines on UTIs prevention and treatment	Setting: 39 NHs (Finland) Period: Guideline creation 1 year and 3 annual point prevalence surveys Design: Before-After controlled study	Other actions: Diagnosis: Drawing local guidelines	UTI prophylaxis: significant decrease from 14.5% pre-intervention to 7.8% at year 2 (p<0.001) UTI treatment: no significant difference (2.1% to 1.7% at year 2, p=0.19)	Fair
Fleet et al. (2014) ¹¹	To evaluate the impact of a Resident Antimicrobial Management Plan (RAMP) on systemic antibiotic use in NHs	Setting: 30 NHs (UK) Period: 5 months pre-intervention ; 5 months post intervention Design: cluster randomized controlled study	Other actions: RAMP tool: Assessment/Communication: 2 parted pre-printed form “initiation of treatment” and “review of treatment” (48h-72h) completed by nurses + support pack (signs and symptoms in the elderly, collecting clinical specimens and information on antimicrobial resistance)	Total antibiotic consumption: decrease of 4.9% in the IG (CI95% 1.0%, 8.6%) (p=0.02) vs increase of 5.1% in the CG (CI95% 0.2%, 10.2%) (p=0.04) Prevalence of systemic antibiotic prescribing: no significant difference between the IG (6.46% pre-intervention, 6.52% post intervention, p=0.94) and the CG (pre-intervention 5.27%, post intervention 5.83%, p=0.4)	Good

Furuno et al. (2014) ¹²	To assess the effect of skilled nursed facility specific antibiograms on empirical antibiotic prescribing	Setting: 1 skilled nursed facility (USA) Period: Pre-intervention 6 month ; post intervention 6 months Design: Before-after uncontrolled study	Other action: Facility specific antibiogram created using WHONET + toolkit education	Prevalence of appropriate empirical antibiotic prescribing: not significant increase from 32% pre-intervention to 45% post-intervention (p=0.32)	Poor
Zimmerman et al. (2014) ¹³	To determine whether antibiotic prescribing can be reduced using a quality improvement programme	Setting: 12 NHs (USA) Period: 3 months baseline & 6 months post intervention Design: Before-after controlled study	Multifaceted intervention: Education: for providers (half day) and nursing staff (90 min.) + pocket cards + informational brochure related to antibiotic prescribing for residents and family Other actions: Communication: medical care referral form Feedback & reporting: guideline-adherent prescriptions, overall prescribing rates (monthly)	Total antibiotic rate for all indications: decrease in intervention group (IRR = 0,86 IC 0.79-0.95 p=0.02) Prescribing rate for respiratory indication: decrease in the IG (IRR=0.71, IC95% 0.56, 0.90, p=0.005) No difference in prescribing rates for urinary tract infections or skin and soft tissue infections between IG and CG.	Fair
Doernberg et al. (2015) ¹⁴	To assess the effect of an antimicrobial stewardship programme on UTI treatment	Setting: 3 NHs (USA) Period: 7 months pre-intervention and 7 months post intervention Design: quasi-experimental uncontrolled study	Multifaceted intervention: Monitoring & surveillance: antimicrobial susceptibilities and antimicrobial utilization Available expertise on infection management: On-site visits by the ID pharmacist to review patients receiving antibiotics for UTIs and formulated recommendations with the ID physician to the prescriber	Antibiotic initiations for UTI (interrupted time series analysis): immediate decrease of 26% (p<0.001), 6% decrease for UTI per month throughout the intervention (p<0.001) Antibiotic initiations for all indications (interrupted time series analysis): immediate intervention change 25% reduction (p<0.0001) and 5% decrease per month throughout the intervention (p=0.001) No significant change in <i>Clostridium difficile</i> infections or multi-drug resistant organisms rates	Fair
Trautner et al. (2015) ¹⁵	To evaluate the effectiveness and sustainability of an intervention to improve catheter-associated ASB management	Setting: 2 Veterans Affairs Medical Centers (USA) Period: Baseline 12 months , Intervention 12 months and Maintenance 12 months Design: Before-after controlled study	Multifaceted intervention: Monitoring & surveillance: incidence of asymptomatic bacteriuria screening and overtreatment Other actions: Development of local guidelines for ASB and catheter-associated urinary tract infection diagnosis + algorithms Education: for physicians, nurses and nurse assistants; case presentations Feedback & reporting	Number of urine culture sent (per 1000 bed-days): significant decrease during intervention and maintenance period compared to baseline in the IG (baseline 41.2, intervention: 23.3 (IRR,0.57;95%CI 0.53-0.61;p<0.001), maintenance: 12.0 (IRR,0.29;95%CI 0.26-0.32;p<0.001)) ; stable over time in the CG Overtreatment of ASB in long term care setting (per 1000 bed-days): Significant difference in the IG (baseline 1.6, intervention 0.6 (IRR,0.35;95%CI 0.22-0.55;p<0.001), maintenance 0.4 (IRR,0.24;95%CI 0.13-0.42;p<0.001)) ; stable over time in the CG No difference between intervention and control group for catheter-associated urinary tract infection undertreatment	Fair

Van Buul et al. (2015)¹⁶	To evaluate the effect of a tailored antibiotic stewardship programme on antibiotic prescribing appropriateness in NHs	<u>Setting:</u> 10NHs (Netherlands) <u>Period:</u> pre-intervention 8 months, intervention 4 months, post intervention 8 months <u>Design:</u> Mixed-methods quasi-experimental controlled study	Implementation of a multifaceted intervention using a PAR (Participatory Action research) approach including: Education: guidelines for physicians and nursing staff education Other actions: Physician-nursing staff communication + Optimizing medication formulary + Utilization of diagnostic resources Monitoring & surveillance: Local UTI resistance patterns	Appropriateness of antibiotic prescribing decisions: - No difference between IG and CG: OR=0.76 (CI95%: 0.43-1.34) - No significant difference pre/post test in IG (82%/79% ; p=0.28) - No significant difference pre/post test in CG (70%/77% ; p=0.06) Total day defined doses (per 1000 resident care-days): - Intervention group: -2.3 (-11.4, +6.8) - Control group: +1.1 (-13.1, +18.2) Guideline-adherent antibiotic selection: - UTI with catheter: +15.9% IG, +1.8% CG - UTI without catheter: +8.3% IG, +5.1 CG - Respiratory tract infections: +0.8% IG, +1.6% CG	Fair
Kassett et al. (2016)¹⁷	To assess the effect of a multifaceted ASP on prescribing practice in a long-term care environment	<u>Setting:</u> 1 LTCF in a geriatric health care facility (Canada) <u>Period:</u> pre-intervention 12 months ; post intervention 12 months <u>Design:</u> Before-after uncontrolled study	Multifaceted intervention: Accountability & responsibilities: ASP team: 1 pharmacist and 2 family medicine physicians Education: presentations, posters, newsletters and handouts; directed to nursing staff, physicians, pharmacists + Residents/families education Other actions: treatment algorithms Monitoring & surveillance Feedback & reporting	Difference in overall antibiotic use (using UTI rate) (per 1000 resident days): no significant difference - 0.048 pre intervention, 0.043 post intervention (p=0.22) Physician prescribing behavior (per 1000 resident days): significant decrease in prescribed days of therapy from 0.27 pre intervention to 0.236 post intervention (p=0.03) Ciprofloxacin rates (per 1000 resident days): significant decrease from 0.014 to 0.006 post intervention (p=0.001).	Poor
McMaughan et al. (2016)¹⁸	To evaluate the impact of a decision-making aid on antibiotic prescriptions for UTIs	<u>Setting:</u> 12 NHs (USA) <u>Period:</u> 6 months pre-intervention & 6 months post-intervention <u>Design:</u> Before-after controlled study with 3 groups (high intensity training, low intensity training, comparison)	Other actions: Aid-making decision for UTI prescription improving communication between physicians and nursing staff + Education about the tool: - High intensity training: two training sessions + active technical support - Low intensity training: one training session + passive technical support.	Proportion of prescription for ASB: - Decreased in high intensity NH from 65% to 57% and low intensity NH from 78% to 65% but increased in comparison homes from 69% to 71.2% post intervention. - Group-analysis according to effective decision-making aid fidelity: high fidelity (4NHs) decrease from 73% to 49% and low fidelity (8 NHs) stable 69.6% to 68.8% post intervention. Likelihood of antibiotic prescription for ASB in IG vs CG : OR 0.35 (95CI 0.16-0.76)	Fair

ASB: asymptomatic bacteriuria; ASP: antimicrobial stewardship programme; CG: control group; ID: infectious diseases; IG: intervention group; LTCF: long term care facility; NH: nursing home; UTI: urinary tract infection

Bold font: main objective of the study when identified

^a The level of evidence was assessed based on the study design: good for randomized controlled studies, fair for controlled before-after studies and poor for uncontrolled before-after studies.

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APPENDIX B – DETAILED INFORMATION ON THE 8 INCLUDED REVIEWS

Reference	Aim	Methodology and quality assessment	Recommendations	Perspectives
Fleming et al. (2013)¹	Systematic review of interventional studies that aim to improve the quality of antibiotic prescribing in long term care setting	Inclusion: randomized controlled trials and cluster randomized controlled trials on 8 databases from inception to August 2012 testing ASPs in LTCFs Quality assessment: Cochrane Collaboration’s “Risk of Bias Table” Results: 4 studies included Mulrow criteria : 8/8	<ul style="list-style-type: none"> - Accountability & responsibilities: identification of a local champion + nurses role in infection management - Education - Other actions: local guidelines - Feedback & reporting - + Repeat interventions for sustainability ; Interest of focusing on one antibiotic class 	Need for appropriate randomization procedures and patient-related outcomes evaluation (drug adverse events or antimicrobial resistance)
Nicolle et al. (2014)²	Review of current evidence on the effectiveness of antimicrobial stewardship interventions in LTCFs	Inclusion: studies published between Jan. 2001 and Jan. 2013 extracted from Medline and EMBASE Results: 9 studies included Mulrow criteria: 5/8	<ul style="list-style-type: none"> - Available expertise on infection management - Education - Other actions: local guidelines - Feedback & reporting 	Current evidence is insufficient to support recommendations for a specific intervention Future studies should explore antimicrobial resistance, <i>Clostridium difficile</i> colitis and cost-effectiveness impact of ASPs

<p>Crnich et al. (2015)³</p>	<p>Narrative review about optimizing antibiotic stewardship in nursing homes</p>	<p>Inclusion: no formal search strategy, inclusion of PubMed articles related to ASPs in LCTFs available until Apr. 2015</p> <p>Results : 14 studies included.</p> <p>Mulrow criteria: 4/8</p>	<ul style="list-style-type: none"> - Management leadership - Accountability & responsibilities: local policies for ASP - Education: for nursing staff, physicians, residents and families - Other actions: local guidelines + facility-specific antibiogram - Monitoring and surveillance: infections, antibiotic use - Feedback & reporting 	<p>Need for studies to evaluate the effects of stewardship interventions on facility and resident outcomes</p>
<p>Dyar et al. (2015)⁴</p>	<p>Narrative review of specific challenges of antimicrobial stewardship implementation in LTCFs and suggestions for improvement</p>	<p>Inclusion : no database or time limit</p> <p>Results : 12 studies included</p> <p>Mulrow criteria: 4/8</p>	<ul style="list-style-type: none"> - Management leadership - Accountability & responsibilities - Education: for nursing staff, physicians, residents and families - Other actions: local guidelines and diagnostic tools + target areas where antibiotic misuse is common + antibiotic time out + computerized decision support - Monitoring & surveillance 	<p>Future studies should explore the contribution of a multidisciplinary antimicrobial management team, computerized decision support and point-of-care diagnostic tests</p>
<p>Morrill et al. (2016)⁵</p>	<p>Review of literature describing antimicrobial stewardship efforts in long term care</p>	<p>Inclusion: studies extracted from Medline between 1966 and June 2015 + follow up internet search</p> <p>Results: 15 studies included</p> <p>Mulrow criteria: 4/8</p>	<ul style="list-style-type: none"> - Management leadership: financial support - Accountability & responsibilities: local leader + pharmacist role + written antimicrobial stewardship policy - Available expertise on infection management - Education - Other actions: facility-specific antibiogram + diagnostic tools - Monitoring & surveillance - Feedback & reporting 	<p>Healthcare utilization, costs, resistances, clinical outcomes or sustainability should be investigated instead of antimicrobial consumption</p>

<p>Katz et al. (2017)⁶</p>	<p>Integrative literature review analyzing antimicrobial stewardship interventions in LTCFs within the framework of a human factors engineering approach</p>	<p>Inclusion: studies published in English that described antimicrobial stewardship in LTCFs and used quantitative outcomes on PubMed Quality assessment: using pre-defined criteria developed by the National Institute of Health Results: 20 studies included Mulrow criteria: 8/8</p>	<ul style="list-style-type: none"> - Management leadership - Available expertise on infection management: external consultants with expertise in ID - Education: multidisciplinary education supported by enduring material - Other actions: Pre-prescriptive data collection tools into nurses' workflow (communication) + Post prescriptive recommendations into prescribers' workflow 	<p>Technology should be incorporated in antimicrobial stewardship programmes (aid-decision making tools or telemedicine for infection management expertise)</p>
<p>Feldstein et al. (2018)⁷</p>	<p>Systematic review evaluating if ASP in NH can reduce health outcomes and lower rates of healthcare utilization</p>	<p>Inclusion: English language randomized controlled trials, non-randomized trials and observational studies of eligible interventions on Pubmed/Medline, Cochrane library, EMBASE and CINAHL from database inception to Feb. 2017 Exclusion: studies assessing interventions focused on one single component of an ASP Quality assessment: using pre-defined criteria developed by the National Institute of Health Results: 14 studies included Mulrow criteria: 8/8</p>	<ul style="list-style-type: none"> - Education: for nursing staff, physicians, residents and families 	<p>Future studies should have longer post intervention period in order to measure resident-related outcomes and not only antimicrobial use or guideline adherence</p>

Falcone et al. (2018) ⁸	Systematic review of studies describing the antimicrobial consumption and evaluating ASPs in LTCFs	Inclusion: studies published in English in the last 10 years on MEDLINE Quality assessment: GRADE; TREND and CONSORT for guideline adherence of the studies Results : 14 studies included Mulrow criteria: 8/8	<ul style="list-style-type: none"> - Education: multifaceted and multidisciplinary programmes - Other actions: diagnostic algorithms + communication/Assessment tools - Monitoring & surveillance 	Need for high quality designed interventional studies
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ASP: antimicrobial stewardship program; ID : infectious disease ; LTCF: long term care facility; NH: nursing home; UTI: urinary tract infection

Mulrow criteria⁹ for systematic review quality assessment :

- Was the specific purpose of the review stated?
- Were sources and methods of the citation search identified?
- Were explicit guidelines provided that determined the material included in and excluded from the review?
- Was a methodologic validity assessment of material in the review performed?
- Was the information systematically integrated with explication of data limitations and inconsistencies?
- Was the information integrated and weighted or pooled metrically?
- Was a summary of pertinent findings provided?
- Were specific directives for new research initiatives proposed?

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APPENDIX C - INVENTORY OF FREELY-AVAILABLE TOOLS TO IMPLEMENT AN ANTIMICROBIAL STEWARDSHIP PROGRAMME IN A NURSING HOME

1. Management leadership towards antimicrobial stewardship

Institution	Description	Format	Weblink
Agency for Healthcare Research and Quality (USA) - 2016	Draft policies and procedures for an antimicrobial stewardship programme	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/3_TK1_T5-Draft_Policies_and_Procedures_for_the_Antimicrobial_Stewardship_Program_final.pdf
Center for Disease Control and prevention (USA) - 2015	Creating a culture to improve antibiotic use in nursing homes	Fact sheet	https://www.cdc.gov/longtermcare/pdfs/Factsheet-Core-Elements-Creating-Culture-Improve-Use.pdf
Minnesota Health Department (USA) - 2019	Communicate antibiotic stewardship priorities	Letter	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/abxproviderletter.pdf
National Center for Antimicrobial Stewardship (Australia) - 2018	Antimicrobial stewardship policy for aged care homes and principles of antimicrobial management	Fact sheet	https://irp-cdn.multiscreensite.com/d820f98f/files/uploaded/AMS%20Policy_Sept%2018.pdf

2. Accountability and responsibilities

Institution	Description	Format	Weblink
Agency for Healthcare Research and Quality (USA) - 2016	Creation of an antimicrobial stewardship team	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/3_TK1_T1-Gather_a_Team_final.pdf
	Implementation planning sample agenda	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/3_TK1_T4-Implementation_Planning_Sample_Agenda_final.pdf
	Role and responsibilities of each professional	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/3_TK1_T2-Roles_and_Responsibilities_final.pdf
Antimicrobial Resistance (Australia) - 2017	What health professionals can do (about antimicrobial resistance)	Poster	https://www.amr.gov.au/resources/infographic-what-health-professionals-can-do
	Explanation of nurses role in antimicrobial stewardship	Fact sheet	https://www.amr.gov.au/resources/nurses-and-amr
Center for Disease Control and prevention (USA) - 2015	Leading antibiotic stewardship in nursing homes	Fact sheet	https://www.cdc.gov/longtermcare/pdfs/Factsheet-Core-Elements-Leading-Antibiotic-Stewardship.pdf
Société de Pathologie Infectieuse de Langue Française (France) - 2013	Missions defined for each professional for antimicrobial stewardship (chapter 3)	Booklet	http://www.mobiquial.org/wordpress/wp-content/uploads/2013/10/RI-Plaquette-32-pages-V6.pdf

3. Available expertise on infection management

Institution	Description	Format	Weblink
-	-	-	-

4. Education and practical training

a- Professionals

Institution	Description	Format	Weblink
Agency for Healthcare Research and Quality (USA) -2016	Training modules for nurses about urinalysis and UTI	Handout	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK1_T4-Urinalysis_and_UTIs_Improving_Care_Final.pdf
Alberta Health services (Canada) / Do bugs need drugs? - 2014	Nurse educator slides (UTI)	Slideshow	http://www.dobugsneeddrugs.org/wp-content/uploads/uti-in-ltc-for-nurse-educators-slides.pdf
	Nurse educator speaking notes (UTI)	Handout	http://www.dobugsneeddrugs.org/wp-content/uploads/uti-in-ltc-for-nurse-educators-with-speaking-notes.pdf
	Nurse educator slides (nursing home-acquired pneumonia)	Slideshow	http://www.dobugsneeddrugs.org/wp-content/uploads/nhap-for-nurse-educators-slides.pdf
	Nurse educator speaking notes (nursing home-acquired pneumonia)	Handout	http://www.dobugsneeddrugs.org/wp-content/uploads/nhap-for-nurse-educators-with-speaking-notes.pdf
Association of Medical Microbiology and Infectious Disease (Canada) - 2016	Symptom-Free pee: let it be presentation (available in English and French)	Slideshow	https://www.ammi.ca/?ID=127&Language=ENG
		Poster	https://www.ammi.ca/Content/AntibioticAwareness/AB-Brief%20poster_Eng_8.5x11_colour.pdf
Antimicrobial Resistance (Australia) - 2017	Online learning modules for health professionals and students (UTI)	Website	https://www.amr.gov.au/what-you-can-do/aged-care/further-education-and-training
British Society for Antimicrobial Chemotherapy (UK) – 2015	Educational course about antimicrobial stewardship	Massive online open course	http://www.bsac-arc.com/#details/11
Minnesota Health Department (USA) - 2019	Educational module: antibiotic use and resistance (for nurses and nursing assistants)	Multi-support	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/aspltc/modprinturseabx.pdf (PDF, nurses) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/aspltc/modslidenurseabx.pdf (Slideshow, nurses) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/aspltc/modanswernurseabx.pdf (Post-test questions, nurses) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/aspltc/modprintnaabx.pdf (PDF, nursing assistants) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/aspltc/modslidenaabx.pdf (Slideshow, nursing assistants) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/aspltc/modanswernaabx.pdf (Post-test questions, nursing assistant)

	Educational module: Urinary tract infections and asymptomatic bacteriuria (for nurses and nursing assistants)	Multi-support	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/modprintnurseuti.pdf (PDF, nurses) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/modslidenurseuti.pdf (Slideshow, nurses) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/modanswernurseuti.pdf (Post-test questions, nurses) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/modprintnauti.pdf (PDF, nursing assistant) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/modslidenauti.pdf (Slideshow, nursing assistant) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/modanswernauti.pdf (Post-test questions, nursing assistant)
	Skills fair game questions	Quiz	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/skillsfairquiznurse.pdf (licensed nurse) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/skillsfairquizstaff.pdf (unlicensed staff)
	Background on antimicrobial stewardship (for providers)	Slideshow	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/slideproviderasp.pdf
	Keep antibiotic working for residents in LTCF	Slideshow	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/slidesnurseasp.pdf
	Antibiotic use & antibiotic resistance	Multi-support	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/coverabx.pdf (cover) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/quizabxflyer.pdf (flyer) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/quizabxtable.pdf (table tent) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/quizabxslides.pdf (slides)
	Urinary tract infections and asymptomatic bacteriuria	Multi-support	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/coveruti.pdf (cover) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/quizutiflyer.pdf (flyer) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/quizutitable.pdf (table tent) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/quizhandslides.pdf (slides)
OMEDIT Bretagne (France) - 2015	e-learning about UTIs in LTCF	E-learning	http://www.omeditbretagne.fr/omeditelearning/infections_urinaires/SCO_0001/multi_launch.html
Société de Pathologie Infectieuse de Langue Française (France) - 2012	Frequent situations in infected patients in LTCF	Multi-support	http://www.infectiologie.com/UserFiles/File/medias/_documents/ATB/ehpad/Poster.pdf (poster) http://www.infectiologie.com/UserFiles/File/medias/_documents/ATB/ehpad/depliant-recto-verso.pdf (leaflet) http://www.infectiologie.com/UserFiles/File/medias/_documents/ATB/ehpad/diaporama_seances_formation_EHPAD.pdf (slideshow) http://www.infectiologie.com/UserFiles/File/medias/_documents/ATB/ehpad/guide_animateur_EHPAD.pdf (slideshow) http://www.infectiologie.com/fr/kit-pedagogique-a-l-usage-des-ehpad-cclin-sud-ouest.html (link to videos)
	Educational slideshow for nursing staff on antimicrobial stewardship	Slideshow	http://www.infectiologie.com/fr/recommandations-d-un-groupe-de-travail-omedit-ars-ile-de-france.html
University of Rochester (USA) - 2016	Educational videos/slideshows related to antimicrobial stewardship in nursing homes	Videos	http://www.rochesterpatientsafety.com/index.cfm?Page=For%20Nursing%20Homes

b- Residents and family

Institution	Description	Format	Weblink
Agency for Healthcare Research and Quality (USA) - 2016	Talking with residents to educate them about antibiotics	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/6_TK1_T1-Talking_with_Residents_checklist_version_Final.pdf
	Talking with residents family members	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/6_TK1_T2-Talking_with_Residents_Family_Members_checklist_version_Final.pdf
	Resident information sheet : Antibiotic resistant bacteria	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/6_TK1_T3-Resident_Information_Sheet_Antibiotic-Resistant_Bacteria_Final.pdf
	Be smart about antibiotics	Leaflet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/6_TK1_T4-Be_Smart_About_Antibiotics_Final.pdf
	How antibiotics can cause more harm than good when not needed (UTI)	Leaflet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/6_TK1_T5-Suspect_a_Urinary_Tract_Infection_brochure_MA_Coalition_final.pdf
	Managing patients and families – discussion for staff meeting	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/6_TK1_T6-Managing_Resident_and_Family_Expectations_Final.pdf
Alberta Health services (Canada) / Do bugs need drugs? - 2014	Frequently asked questions – UTI	Leaflet	http://www.dobugsnneeddrugs.org/wp-content/uploads/uti-faq.pdf
	Frequently asked questions – nursing home-acquired pneumonia	Leaflet	http://www.dobugsnneeddrugs.org/wp-content/uploads/nhap-faq.pdf
Association of Medical Microbiology and Infectious Disease (Canada) - 2016	Fillable resident family letter – symptom-free pee: let it be Letter	Form	https://www.ammi.ca/Content/AntibioticAwareness/AB%20form_Eng_colour.pdf
Antimicrobial Resistance (Australia) - 2017	What patients can do (about antimicrobial resistance)	Fact sheet	https://www.amr.gov.au/resources/infographic-what-you-can-do
	Choosing wisely Australia (resources for consumers)	Website	http://www.choosingwisely.org.au/resources/consumers/antibiotic-resources-for-consumers
	NPS Medicine Wise (resources for consumers)	Website	https://www.nps.org.au/medical-info/consumer-info/antibiotics-explained
Center for Disease Control and prevention (USA) - 2015	What to ask your healthcare provider before asking for antibiotics	Leaflet	https://www.cdc.gov/longtermcare/pdfs/factsheet-core-elements-what-to-ask.pdf
	What you need to know about antibiotics in a nursing home	Leaflet	https://www.cdc.gov/longtermcare/pdfs/factsheet-core-elements-what-you-need-to-know.pdf
Minnesota Health Department (USA) - 2019	Sample newsletter article for LTCF	Letter	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/ltsamplearticle.pdf
Saskatchewan Health Authority (Canada) - 2017	UTI & ASB information for patients and families	Handout	http://www.rqhealth.ca/service-lines/master/files/9072573_8_UTI%20Pamphlet%20CEAC%201321.pdf
Société de Pathologie Infectieuse de Langue Française (France) - 2012	Antimicrobial stewardship for frequent situations in LTCF	Leaflet	http://www.infectiologie.com/UserFiles/File/medias/documents/ATB/ehpad/2012-ATB-EHPAD-ARSidf-Depliant-famille.pdf

5. Other actions aiming at responsible antimicrobial use

a- Diagnosis/algorithms

Institution	Description	Format	Weblink
Agency for Healthcare Research and Quality (USA) - 2016	Policy statement for utilization of minimum criteria for infections	Letter	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK3_T1-Sample_Policy_final.pdf
	Minimum criteria for antibiotics	Website	https://www.ahrq.gov/nhguide/toolkits/determine-whether-to-treat/antibiotic-tool.html
	12 situations when antibiotics are not needed	Pocket card	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK2_T2-Antibiotic_Pocket_Cards.pdf
Alberta Health services (Canada) / Do bugs need drugs? - 2014	UTI checklist diagnosis	Leaflet	http://www.dobugsneeddrugs.org/wp-content/uploads/uti-checklist.pdf
	nursing home-acquired pneumonia checklist diagnosis	Leaflet	http://www.dobugsneeddrugs.org/wp-content/uploads/nhap-checklist.pdf
Association of Medical Microbiology and Infectious Disease (Canada) - 2016	UTI diagnosis algorithm	Pocket card	https://www.ammi.ca/Content/AntibioticAwareness/AB-Algorithm_Eng_8.5x11_colour.pdf
Arizona Department of health (USA) - 2014	Asymptomatic bacteriuria and reasons to avoid antimicrobial use	Pocket card	https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/healthcare-associated-infection/advisory-committee/antimicrobial-stewardship/asb-pocketcard.pdf
		Handout	https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/healthcare-associated-infection/advisory-committee/antimicrobial-stewardship/asb-optimizing-use.pdf
Minnesota Health Department (USA) - 2019	Infection surveillance definition worksheet	Form	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/lc/apxk.pdf
	Minimum criteria for initiation of antibiotics in long term care residents	Multi-support	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/lc/abxcard.pdf (pocket card) https://www.health.state.mn.us/diseases/antibioticresistance/hcp/lc/abxcardposter.pdf (poster)
	Asymptomatic bacteriuria	Leaflet	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/lc/asbltc.pdf
	Loeb and McGeer criteria : a practical guidance for use in LTCF	Fact sheet	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/lc/loebmcgeer.pdf
Saskatchewan Health Authority (Canada) - 2017	Differences between ASB and UTI	Poster	http://www.rqhealth.ca/service-lines/master/files/9072574_8_2017_UTI_Poster.pdf

b- Assessment/Communication

Institution	Description	Format	Weblink
Agency for Healthcare Research and Quality (USA) - 2016	Template letter to recommend the SBAR toolkit to clinicians	Letter	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK1_T2-Clinician_letter_Final_0.pdf
	Help patient assessment and communication (SBAR) with prescriber for UTI, low respiratory tract infections and skin/soft tissue infections	Form	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK1_T1-SBAR_UTI_Final.pdf (UTI) https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK3_T2-b-SBAR_LRI_Final.pdf (low respiratory tract infections) https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK3_T2-c-SBAR_SST_Final.pdf (skin/soft tissue infections)
	Rationale for SBAR utilization	Leaflet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK1_T3-Not_all_infections_need_antibiotics_final.pdf
	Medical Care Referral Form to improve assessment and communication	Form	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK2_T1-Medical_Care_Referral_Form.pdf
	Educational lecture to improve communication and patient assessment	Slideshow (available on the website)	https://www.ahrq.gov/nhguide/toolkits/determine-whether-to-treat/toolkit2-communications-and-decisionmaking.html
Minnesota Health Department (USA) - 2019	Nurse process evaluation tool – Resident change in condition	Form	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/apxf.pdf
	Concerned-Uncomfortable-Safety (CUS) communication tool PDF document	Form	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/apxh.pdf
	SBAR tool	Form	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/apxg.pdf
	Resident changes evaluation	Form	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/apxi.pdf
	72-Hour antibiotic time out sample template	Form	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/ltc/abxtimeout.pdf
Nebraska Antimicrobial Stewardship Assessment and Promotion Program (USA) - 2018	SBAR for antibiotic time out	Form	http://www.cidrap.umn.edu/asp/clinicaltools/sbar-tool-antibiotic-time-out
Linnebur (2011)	care pathway for nursing home-acquired pneumonia preprinted orders for patient	Article	Impact of a multidisciplinary intervention on antibiotic use for nursing home-acquired pneumonia DOI : 10.1016/j.amjopharm.2011.09.009

c- Microbiology testing

Institution	Description	Format	Weblink
Association of Medical Microbiology and Infectious Disease (Canada) - 2016	Symptom-free pee: let it be: when to perform urinalysis	Poster	https://www.albertahealthservices.ca/assets/info/hp/as/if-hp-as-symptom-free-pee-let-it-be-poster.pdf
	Criteria for UTI-testing	Pocket card	https://www.albertahealthservices.ca/assets/info/hp/as/if-hp-as-evidence-based-criteria-for-urinary-infection-testing.pdf
Infectio-Lille (France) - 2018	When to perform urine dipstick or urinalysis in older people	Leaflet	http://www.infectio-lille.com/Antibiotiques/Prelevement-Sujet-age-Hdf-2018.pdf
National Center for Antimicrobial Stewardship (Australia) - 2018	Microbiology fact sheets to help with the interpretation of microbiology reports (urine, sputum, wound swab)	Fact sheets	https://irp-cdn.multiscreensite.com/d820f98f/files/uploaded/Microbiology_Fact_Sheet_Urine_MCS.pdf https://irp-cdn.multiscreensite.com/d820f98f/files/uploaded/Microbiology_Fact_Sheet_Sputum_MCS.pdf https://irp-cdn.multiscreensite.com/d820f98f/files/uploaded/Microbiology_Fact_Sheet_Wound_swab_MCS.pdf
National Health Service (UK) - 2017	To Dip or Not To Dip: programme created to improve the management of urinary testing and UTI treatment	Multi-support	http://www.enhertscg.nhs.uk/sites/default/files/TDONTD-Handbook-v4-FINAL.pdf (booklet) http://www.enhertscg.nhs.uk/sites/default/files/To-Dip-or-Not-to-Dip.pdf (leaflet) http://www.enhertscg.nhs.uk/sites/default/files/TDONTD%20NHS%20Poster_Oct20171.pdf (poster) http://www.enhertscg.nhs.uk/urinary-tract-infections-utis-care-homes (care home training and patient assessment available at this address)
Société de Pathologie Infectieuse de Langue Française (France) - 2012	Good practice for microbiology testing	Fact sheet	http://www.infectiologie.com/UserFiles/File/medias/_documents/ATB/ehpad/2012-ATB-EHPAD-ARSidf-Prelevement.pdf
Crnich (2015)	Decision pathway to reduce unnecessary urine testing	Article	Optimizing Antibiotic Stewardship in Nursing Homes: A Narrative Review and Recommendations for Improvement DOI : 10.1007/s40266-015-0292-7
Loeb (2005)	Diagnostic algorithm for ordering urine cultures / treatment algorithm for prescribing antimicrobials	Article	Effect of a multifaceted intervention on number of antimicrobial prescriptions for suspected urinary tract infections in residents of nursing homes: cluster randomized controlled trial DOI : 10.1136/bmj.38602.586343.55
Zabarsky (2008)	Indications for sending urine cultures/criteria for empiric antibiotic treatment/criteria for diagnosis of symptomatic UTI	Article	Sustained reduction in inappropriate treatment of asymptomatic bacteriuria in a long-term care facility through an educational intervention DOI : 10.1016/j.ajic.2007.11.007
Trautner (2015)	Algorithm for CAUTI diagnostic and treatment (eAppendix)	Article	Effectiveness of an Antimicrobial Stewardship Approach for Urinary Catheter-Associated Asymptomatic Bacteriuria DOI : 10.1001/jamainternmed.2015.1878

d- Antibigrams

Institution	Description	Format	Weblink
Agency for Healthcare Research and Quality (USA) - 2016	Sample policy letter to explain the importance of antibigrams	Letter	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK1_T5-Sample_Policy_Letter_final.pdf
	Purpose and use of the antibiogram	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK1_T1-Background_final.pdf
	Guide to working with lab to obtain an antibiogram	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK1_T2-Working_with_a_lab_final.pdf
	Sample letter of agreement with a lab	Letter	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK1_T3-Sample_Letter_of_Agreement_final.pdf
	Antibiogram format and instructions	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK1_T4-Antibiogram_Formats_and_Instructions_final.pdf
	Distribution planning for an antibiogram	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK1_T6-Sample_Distribution_Plan_for_an_Antibiogram_final.pdf
	Concise antibiogram toolkit background	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK2_T1-Concise_Antibiogram_Toolkit_Background.pdf
	Getting started : sources of data for an antibiogram	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK2_T2-Concise_Antibiogram_Toolkit_Getting_Started.pdf
	Using WHONET to create your antibiogram	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK2_T3-Concise_Antibiogram_Toolkit_Using_WHONET_to_Create_Your_Antibiogram.pdf
	How to enter manually into an antibiogram template	Fact sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK2_T4-Concise_Antibiogram_Toolkit_How_to_Enter_Data_Manually_into_an_Antibiogram_Template.pdf
	Comprehensive antibiogram template	Form	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/5_TK2_T5-Concise_Antibiogram_Toolkit_Comprehensive_Antibiogram_Template.pdf
The Antibiogram Program : toolkit including Assessment and planning, development, implementation and monitoring (tools for each part available on the website)	Website	https://www.ahrq.gov/nhguide/toolkits/help-clinicians-choose-the-right-antibiotic/toolkit3-develop-implement-antibiogram-program.html	
Arizona Department of Health (USA) - 2015	Understanding the antibiogram in the long-term care setting	Handout	https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/healthcare-associated-infection/advisory-committee/antimicrobial-stewardship/understanding-the-antibiogram.pdf
Minnesota Health Department (USA) - 2019	General explanations about an antibiogram	Leaflet	https://www.health.state.mn.us/diseases/antibioticresistance/abx/antibiograms.pdf
	Sample letter to obtain an antibiogram from a laboratory	Letter	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/lc/abxlabagreement.pdf

6. Monitoring and surveillance

Institution	Description	Format	Weblink
Agency for Healthcare Research and Quality (USA) -2016	Antibiotic using track sheet	Form	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/3_TK2_T2-Antibiotic_Use_Tracking_Sheet_Final.pdf
Center for Disease Control and prevention (USA) - 2015	Information on how to measure antibiotic stewardship activities, antibiotic uses and antibiotic related outcomes	Booklet	https://www.cdc.gov/longtermcare/pdfs/core-elements-antibiotic-stewardship-appendix-b.pdf
Minnesota Health Department (USA) - 2019	Antimicrobial use assessment	Form	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/lc/apxe.pdf
	Infection and antibiotic use tracking tool + webinar (available on the website) + instruction	Multi-support	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/lc/apxlinstructions.pdf
	Tips for applying CDC's infection surveillance guidance in LTCF	Fact sheet	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/lc/apxi.pdf
European Society of Clinical Microbiology and Infectious Diseases (Europe) – 2019 (v1.9)	AMCTool : programme to calculate antimicrobial consumption	Website	http://amu-tools.org/amctool/amctool.html

7. Reporting and feedback

Institution	Description	Format	Weblink
Agency for Healthcare Research and Quality (USA) -2016	Sample monthly Summary reports to track progression	Form	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/3_TK2_T3-Sample_Monthly_Summary_Reports_Final.pdf
	Prescribing profile for individual prescriber feedback	Form	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/3_TK2_T4-Quarterly_or_Monthly_Prescribing_Profile_Final.pdf
	Quality improvement meetings tip sheet	Tip sheet	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguide/4_TK2_T3-QI_Meetings_Tip_Sheet_final.pdf
Minnesota Health Department (USA) - 2019	Template feedback form for providers	Form	https://www.health.state.mn.us/diseases/antibioticresistance/hcp/asp/lc/abxfeedbackform.pdf
Nebraska Antimicrobial Stewardship Assessment and Promotion Program (USA) - 2018	Sample annual antimicrobial stewardship programme report for LTCF staff	Form	http://www.cidrap.umn.edu/asp/clinicaltools/annual-asp-activity-report-ltcf-staff
	Sample annual antimicrobial stewardship programme report for prescribers	Form	http://www.cidrap.umn.edu/asp/clinicaltools/annual-asp-activity-report-ltcf-prescribers

8. General recommendations for implementation

Institution	Description	Format	Weblink
Agency for Healthcare Research and Quality (USA) - 2016	Guidance to choose the right toolkit based on goals, level of resources and requirements	Website	https://www.ahrq.gov/nhguides/about/choosing-the-right-toolkit.html
	Readiness assessment to help determine what the nursing home is prepared to undertake	Checklist	https://www.ahrq.gov/sites/default/files/wysiwyg/nhguides/3_TK1_T3-Readiness_Assessment_final.pdf
British Society for Antimicrobial Chemotherapy (UK) – 2018	e-book dedicated to antimicrobial stewardship; comprehensive approach on antimicrobial stewardship in LTCF (chap.17)	E-book	http://www.bsac.org.uk/antimicrobialstewardshippebook/BSAC-AntimicrobialStewardship-FromPrinciplestoPractice-eBook.pdf
Center for Disease Control and prevention (USA) - 2015	Core elements of antibiotic stewardship for nursing homes	Booklet	https://www.cdc.gov/longtermcare/pdfs/core-elements-antibiotic-stewardship.pdf
	Policy and Practice Actions to Improve Antibiotic Use	Booklet	https://www.cdc.gov/longtermcare/pdfs/core-elements-antibiotic-stewardship-appendix-a.pdf
	Baseline assessment of policies and practices	Checklist	https://www.cdc.gov/longtermcare/pdfs/core-elements-antibiotic-stewardship-checklist.pdf
Michigan Antibiotic Resistance Reduction coalition (USA) - 2008	Antimicrobial stewardship programme for nursing home (chapter 6,7 & 8 dedicated to use antibiotic wisely)	E-book	http://mi-marr.org/LTC_toolkit.php
Minnesota Health Department (USA) - 2019	Guidance for promoting antimicrobial stewardship in LTCF	Fact sheet	https://www.health.state.mn.us/diseases/antibioticsresistance/hcp/asp/lc/apxa.pdf
	Action steps and strategies	Handout	https://www.health.state.mn.us/diseases/antibioticsresistance/hcp/asp/lc/apxb.pdf
	General recommendations for antimicrobial stewardship	Leaflet	https://www.health.state.mn.us/diseases/antibioticsresistance/hcp/asp/lc/aspltc.pdf
	Antimicrobial stewardship gap analysis	Form	https://www.health.state.mn.us/diseases/antibioticsresistance/hcp/asp/lc/apxc.pdf
	Antibiotic use beliefs survey	Survey	https://www.health.state.mn.us/diseases/antibioticsresistance/hcp/asp/lc/apxd.pdf
Nebraska Antimicrobial Stewardship Assessment and Promotion Program (USA) - 2018	Implementation of antimicrobial stewardship components stratified by level of resources	Fact sheet	https://asap.nebraskamed.com/wp-content/uploads/sites/3/2017/07/ASP-strategy-implementation-stratified-by-resource-LTCF.pdf
Washington State Department of Health (USA) – 2018	JumpStart Stewardship: programme implementation for antimicrobial stewardship	E-book	https://www.doh.wa.gov/Portals/1/Documents/5000/420-Non-DOH-JumpStartStewardshipNursingHomes.pdf
	Implementation plan	Form	http://www.cidrap.umn.edu/asp/clinicaltools/antimicrobial-stewardship-implementation-plan
	EQuIP for long term care facilities : full programme for antimicrobial stewardship	Multi-support	https://www.doh.wa.gov/YouandYourFamily/InfluenzaandDisease/HealthcareAssociatedInfections/EQuIP/LongTermCare
Jump (2017)	Antibiotic stewardship implementation and policy (Box1)	Article	Template for an Antibiotic Stewardship Policy for Post-Acute and Long-Term Care Settings DOI: 10.1016/j.jamda.2017.07.018

ASB: asymptomatic bacteriuria; CDI: *Clostridium difficile* Infection; LTCF: long term care facility; OMEDIT: observatoire des médicaments, dispositifs médicaux et innovation thérapeutique; SBAR: Situation, Background, Assessment, Request; UTI: urinary tract infection

ANNEXE D : QUESTIONNAIRE DE L'ENQUETE ANTIBIOEHPAD

Stratégie de bon usage des antibiotiques en EHPAD

A) Questions préliminaires

1. Nom de l'établissement : ; Commune :

Numéro FINESS de l'établissement : ; Adresse mail :

2. L'option tarifaire de votre établissement est :

- un tarif partiel sans pharmacie à usage intérieur (PUI)
- un tarif partiel avec PUI
- un tarif global sans PUI
- un tarif global avec PUI

B) Pratiques de prise en charge des infections

3. Avez-vous un(des) référent(s) infections/antibiotiques pour votre établissement ?

- OUI
- NON

Si oui, rôle(s) de ce(s) référent(s) (plusieurs réponses possibles) :

- Conseils sur le diagnostic des infections
- Conseils sur la prise en charge thérapeutique des infections
- Suivi du bon usage des antibiotiques
- Suivi de l'écologie bactérienne de votre établissement
- Autre(s), préciser :

Profession du(des) référent(s) :

Temps global dédié à l'activité de référent : ETP

Avez-vous un(des) protocole(s) écrit(s) concernant la démarche diagnostique des patients suspects d'infection ? (plusieurs réponses possibles)

- Oui pour les médecins
- Oui pour les infirmiers
- Non

4. Avez-vous un(des) document(s) écrit(s) de protocole ou mode opératoire concernant les examens et les aspects suivants :

	Bandelette urinaire (BU)	Examen cytbactériologique des urines (ECBU)	Hémocultures
les indications de réalisation	<input type="checkbox"/> oui <input type="checkbox"/> non	<input type="checkbox"/> oui <input type="checkbox"/> non	<input type="checkbox"/> oui <input type="checkbox"/> non
les modalités pratiques de prélèvement	<input type="checkbox"/> oui <input type="checkbox"/> non	<input type="checkbox"/> oui <input type="checkbox"/> non	<input type="checkbox"/> oui <input type="checkbox"/> non
l'interprétation des résultats quant au diagnostic d'infection	<input type="checkbox"/> oui <input type="checkbox"/> non	<input type="checkbox"/> oui <input type="checkbox"/> non	<input type="checkbox"/> oui <input type="checkbox"/> non
l'interprétation des résultats quant à la décision d'antibiothérapie	<input type="checkbox"/> oui <input type="checkbox"/> non	<input type="checkbox"/> oui <input type="checkbox"/> non	<input type="checkbox"/> oui <input type="checkbox"/> non

5. Mettez-vous à disposition des prescripteurs dans votre établissement des guides de prescription sous format papier ou électronique pour aider au choix antibiotique (indication, molécule, posologie, durée de traitement) dans les infections courantes (infections urinaires, pulmonaires et cutanées) ? (plusieurs réponses possibles)

→ NON

→ OUI ; si oui, préciser : Antibioguide

→ Antibioville

→ Antibioclic

→ Autre ; préciser :

6. L'information concernant ANTIBIOTEL est-elle diffusée auprès des prescripteurs dans votre établissement (service gratuit d'AntibioEst, qui permet de joindre un infectiologue au téléphone en semaine pour un avis) ?

OUI

NON

7. Y-a-t-il une directive de l'établissement pour que les prescripteurs renseignent indication, molécule, posologie et durée de chaque antibiothérapie dans le dossier patient lors de l'initiation d'un traitement ?

OUI

NON

8. Y-a-t-il une directive de l'établissement de réévaluation systématique des antibiothérapies ? (plusieurs réponses possibles)

OUI à 48-72 heures

OUI à J7

NON

9. Avez-vous organisé au cours des 3 dernières années des formations sur les infections/l'antibiothérapie dans votre établissement ? (plusieurs réponses possibles)

OUI à destination des médecins généralistes

OUI à destination du personnel infirmier

NON

10. Avez-vous réalisé au cours des 3 dernières années une évaluation des pratiques sur le thème des infections/de l'antibiothérapie dans votre établissement ?

OUI

NON

11. Avez-vous accès aux données de consommation antibiotique (au minimum annuelles) de votre établissement ?

OUI

NON

12. Avez-vous accès aux données d'épidémiologie bactérienne (au minimum annuelles, type de bactéries et profil de sensibilité, par exemple dans les urines) de votre établissement ?

OUI

NON

13. Utilisez-vous d'autres stratégies pour promouvoir le bon usage des antibiotiques dans votre établissement ?

OUI ; si oui, préciser :

NON

C) Perceptions sur l'antibiothérapie

Parmi les affirmations suivantes, choisissez la réponse de votre choix sachant que :

- 0 : pas du tout d'accord, absence d'intérêt ou absence d'effet

- 5 : tout à fait d'accord, intérêt maximal ou effet maximal

Affirmations	Réponses
15. Le bon usage des antibiotiques est un enjeu majeur de santé publique	0 1 2 3 4 5
16. Il est souhaitable que le bon usage des antibiotiques devienne un axe prioritaire de la politique de notre établissement dans les prochaines années	0 1 2 3 4 5
<p>17. Les personnes suivantes pourraient influencer les pratiques de prescription des antibiotiques au sein de notre établissement :</p> <p>1. Les résidents</p> <p>2. L'entourage des résidents</p> <p>3. Le médecin coordonnateur de l'établissement</p> <p>4. L'infirmier coordonnateur de l'établissement</p> <p>5. Les différents médecins généralistes des résidents</p> <p>6. D'autres prescripteurs intervenant dans l'établissement (médecins d'autres spécialités, dentistes...)</p>	<p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p>

7. L'équipe infirmière de l'établissement	0	1	2	3	4	5
8. Le directeur de l'établissement	0	1	2	3	4	5
9. Le(s) laboratoire(s) de biologie médicale intervenant pour l'établissement	0	1	2	3	4	5
10. Le(s) pharmacien(s) d'officine intervenant pour l'établissement	0	1	2	3	4	5
11. Autre (préciser) :	0	1	2	3	4	5

D) Opportunités d'amélioration

Parmi les affirmations suivantes, **quelles seraient selon vous les actions les plus efficaces sachant que :**

- 0 : absence d'effet
- 5 : effet maximal

Affirmations	Réponses
18. Une chartre d'engagement du bon usage de l'antibiothérapie affichée dans l'établissement	0 1 2 3 4 5

<p>19. L'instauration de séances de formation et informations sur les principes de bon usage des antibiotiques à destination :</p> <p>1. Des médecins des résidents</p> <p>2. Des infirmiers</p> <p>3. Des aide-soignants</p> <p>4. Des résidents</p> <p>5. De l'entourage des résidents</p> <p>6. Du Médecin coordonnateur</p> <p>7. De l'infirmier coordonnateur</p> <p>8. Autre (préciser) :</p>	<p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p>
<p>20. L'instauration de séances de formation sur les examens complémentaires de microbiologie concernant :</p>	
<p>1. Les indications</p> <p>2. La réalisation</p> <p>3. L'interprétation</p>	<p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p> <p>0 1 2 3 4 5</p>
<p>21. La diffusion de guides de prescription d'aide à la prescription d'antibiothérapie</p>	<p>0 1 2 3 4 5</p>

22. La précision écrite systématique de l'indication, voie d'administration, posologie et durée de l'antibiothérapie dans le dossier patient	0	1	2	3	4	5
23. Le création d'indicateurs évaluant la pertinence des consommation d'antibiotiques	0	1	2	3	4	5
24. Le création d'indicateurs évaluant la pertinence des prescriptions d'examen microbiologiques	0	1	2	3	4	5
25. L'organisation d'évaluation des pratiques (audit) dans l'établissement	0	1	2	3	4	5
26. La communication des résultats de quantité d'antibiotiques prescrits pour les résidents de l'établissement aux équipes médicales et paramédicales en comparaison avec les autres établissement	0	1	2	3	4	5
27. La communication des résultats d'épidémiologie bactérienne de l'établissement aux équipes médicales et paramédicales en comparaison avec les autres établissement	0	1	2	3	4	5

Autres suggestions pour améliorer l'usage des antibiotiques en EHPAD (texte libre) :

.....

.....

.....

.....

.....

.....

E) Caractéristiques de l'EHPAD

28. Votre établissement fait-il partie d'un groupe gestionnaire d'EHPAD ?

- non
 oui ; si oui, quel groupe :_.....

29. Votre établissement dispose (plusieurs réponses possibles) :

- d'un médecin coordinateur
 d'un infirmier coordinateur / d'un cadre de santé
 aucune des deux

30. Votre établissement dispose (plusieurs réponses possibles) :

- d'un rattachement à un centre hospitalier
→ d'une convention avec une pharmacie d'officine donnée
→ d'une convention avec un laboratoire d'analyses médicales
→ aucune des réponses précédentes

31. Personnel soignant employé au sein de votre établissement :

/_/_/_/ équivalent-temps plein (ETP) de médecins

/_/_/_/ ETP d'infirmiers /_/_/_/ ETP d'aides-soignants

32. Personnel médical libéral (vacataires) intervenant au sein de votre établissement :

/_/_/_/ (nombre de) médecins généralistes

33. Informatisation de votre établissement :

1. Les dossiers médicaux des résidents sont informatisés :

- non oui, partiellement oui, complètement

2. Les prescriptions médicamenteuses sont informatisées :

- non oui, partiellement oui, complètement

3. Les prescriptions des antibiotiques (systémiques) sont informatisées :

- non oui, occasionnellement/certaines prescriptions
 oui, systématiquement/toutes prescriptions

34. Date de réalisation du questionnaire :/...../.....

35. Professionnels ayant rempli le questionnaire :

- médecin coordonnateur
- infirmier coordonnateur
- les 2
- autre ; précisez :.....

ANNEXE E : LETTRE D'INVITATION AUX EHPAD POUR L'ENQUETE ANTIBIOEHPAD



Nancy, le 28/05/19

A l'attention du médecin et de l'infirmier coordonnateurs,

L'équipe de recherche ANTIBIOVAC (Université de Lorraine), en collaboration avec AntibioEst, l'Agence Régionale de Santé (ARS) Grand Est, l'Observatoire des Médicaments, Dispositifs médicaux et Innovations Thérapeutiques (OMEDIT) Grand Est et la Direction Régionale du Service Médical (DRSM) Grand Est lancent la première enquête régionale sur les stratégies visant à améliorer l'utilisation des antibiotiques en EHPAD. Les résultats serviront à orienter la politique de santé régionale et nationale sur ce sujet. Nous vous serions reconnaissants de votre participation.

Notre objectif est de décrire les pratiques actuelles concernant l'usage des antibiotiques dans les EHPAD de la région Grand Est et de connaître votre avis quant aux meilleures stratégies à adopter pour promouvoir le bon usage.

Nous souhaiterions que le médecin et l'infirmier coordonnateurs de chaque EHPAD répondent à cette enquête de manière conjointe afin d'obtenir l'image la plus proche de la réalité.

Le temps de réponse estimé pour le questionnaire est d'environ 20 minutes. Vous trouverez en pièce jointe de ce mail le format PDF du questionnaire pour vous permettre de préparer les réponses en amont. Pour répondre à l'enquête en ligne, il suffit de cliquer sur le lien suivant :

<https://fr.surveymonkey.com/r/QRDCHM5>

Nous recueillons le nom de l'EHPAD pour des raisons logistiques, mais l'analyse et la publication des résultats se fera en respectant l'anonymat complet. Nous nous engageons également à vous restituer les résultats globaux de l'enquête, une fois celle-ci terminée.

Nous vous remercions par avance pour votre participation.

Bien cordialement,

Le comité scientifique de l'enquête régionale antibioEHPAD :

- Pr Céline Pulcini (infectiologue, co-coordonnatrice de l'axe ANTIBIOVAC, Nancy)
- Pr Nathalie Thilly (épidémiologiste, co-coordonnatrice de l'axe ANTIBIOVAC, Nancy)
- Pr Nelly Agrinier (épidémiologiste, ANTIBIOVAC, Nancy)
- Pr Jean-Marc Boivin (médecin généraliste, AntibioEst, Nancy)
- Dr Alexandre Charmillon (infectiologue, coordonnateur d'AntibioEst, Nancy)
- Dr Virginie Chopard (pharmacien, Omédit Grand Est, Nancy)
- Dr Véronique Hansmann (médecin généraliste, ARS Grand Est, Strasbourg)
- Dr Ouarda Pereira (économiste, DRSM Nord-Est, Nancy)
- Dr Claudine Dif (pharmacien, DRSM Nord-Est, Nancy)
- Dr Damien Gonthier (médecin généraliste, Nancy)
- Yosra Mouelhi (Post-Doc, ANTIBIOVAC, Nancy)
- Martin Belan (interne, Nancy)

Si vous avez des questions, n'hésitez pas à nous contacter :

Martin Belan : m.belan@chru-nancy.fr



RÉSUMÉ DE LA THÈSE

Contexte : La prescription d'antibiotiques et l'antibiorésistance sont des problématiques de plus en plus fréquentes dans les EHPAD. Bien que l'intérêt des programmes de bon usage des antibiotiques (BUA) ne soit plus à démontrer en milieu hospitalier, la preuve de leur efficacité et leur mise en place dans les EHPAD restent insuffisantes.

Méthodes : Nous avons réalisé une revue systématique de littérature à partir de la base de données MEDLINE incluant les études interventionnelles, revues de littérature, avis d'experts et recommandations relatives au BUA en EHPAD. Nous avons effectué une recherche sur les sites des sociétés savantes et agences officielles de santé ainsi qu'une enquête d'experts pour recenser les outils disponibles gratuitement pour aider au développement de programme de BUA en EHPAD. Nous avons également réalisé une enquête régionale dans les EHPAD de la région Grand Est sur les stratégies de BUA mises en place et les opportunités d'amélioration.

Résultats : 36 études ont été incluses dans notre revue de littérature. La majorité des études interventionnelles étaient réalisées en Amérique du Nord et étudiaient la mise en place d'interventions multiples, montrant une amélioration du respect des recommandations et une diminution des consommations d'antibiotiques ou des examens de microbiologie inutiles. 156 outils ont été recensés dont la plupart étaient relatifs à des stratégies d'éducation, d'évaluation des résidents ou de surveillance. 75 (18%) EHPAD ont répondu à notre enquête sur les pratiques relatives au BUA, avec des stratégies mises en place dans la quasi-totalité des établissements répondants. Les perceptions sur le sujet étaient plutôt bonnes et la mise en place de stratégies de BUA semblait importante dans l'avenir pour les établissements.

Conclusion : La mise en place de programmes de bon usage des antibiotiques est nécessaire et doit être intensifiée dans les EHPAD, d'autant plus que la problématique de l'antibiorésistance et l'intérêt des programmes de BUA semblent bien compris.

Antibiotic stewardship in nursing homes : a systematic review, an inventory of tools and a regional assessment survey.

THÈSE : MÉDECINE SPÉCIALISÉE – ANNÉE 2020.

MOTS CLES : bon usage des antibiotiques; antibiorésistance; EHPAD; revue de littérature; outils; enquête.

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