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Article

A Novel GPPAS Model: Guiding the Implementation of Antimicrobial Stewardship in Primary Care Utilising Collaboration between General Practitioners and Pharmacists

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Abstract: Interprofessional collaboration between general practitioners (GPs) and community pharmacists (CPs) is central to implement antimicrobial stewardship (AMS) programs in primary care. This study aimed to design a GP-pharmacist antimicrobial stewardship (GPPAS) model in Australian primary care. A seven-component exploratory study was conducted since 2017 to 2021 to inform a GPPAS model. We generated both secondary and primary evidence through a systematic review, a scoping review, a rapid review, nationwide surveys of Australian GPs and CPs including qualitative components and a pilot study of a GPPAS model. All study evidence was synthesised, reviewed, merged and triangulated to design a prototype GPPAS model using a Systems Engineering Initiative for Patient Safety theoretical framework. Secondary evidence informed effective GPPAS interventions, and primary evidence captured interprofessional issues, challenges and future needs to implement GPPAS interventions by GPs and CPs. A GPPAS model framework involving GP-pharmacist team-based five GPPAS sub-models were successfully designed to foster AMS education, antimicrobial audits, diagnostic stewardship, delayed prescribing, and routine review of antimicrobial prescription by improved GP-CP collaboration. A GPPAS model could be used as a guide to collaboratively optimise antimicrobial use by GPs and CPs. Implementation studies on GPPAS model and sub-models are required to integrate GPPAS model into GP-pharmacist interprofessional care models in Australia.

Keywords: antimicrobial stewardship; implementation model; GP-pharmacist collaboration; primary care

1. Background

Growing antimicrobial resistance associated with antimicrobial use is an increasing threat to health care and global community [1,2]. Primary care has got much attention for the use, overuse and inappropriate use of antimicrobials for conditions including those that are nonsuggestive of antibiotic therapy [3]. Though primary care patient services vary significantly by country, these services are ubiquitously less-compliant with the concept of team-based antimicrobial care to a patient [4]. The culture of independent antimicrobial use decision by the doctors, pharmacists and patients has become normalised in the society which substantially influences inappropriate use of antimicrobials. The health system structure that promotes a cultural shift to a team-based antimicrobial care is a key

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requirement [5] to drive implementation of antimicrobial stewardship (AMS) programs in primary care.

General practitioners (GPs) and community pharmacists (CPs) are the most important antimicrobial stewards. Their collaboration, co-ordination and communication are central to optimise antimicrobial use in primary care [6,7]. This collaboration is of utmost importance to incorporate and execute AMS programs into routine practices. CPs represent the third largest health care provider groups globally [8], and they are still underutilised resources to implement AMS activities. The World Health Organisation and the Royal Pharmaceutical Society have emphasised the importance of greater involvement and role extension of CPs to foster AMS implementation in primary care. However, those extended roles are neither clearly defined nor policy-guided in many countries national AMS action plans, and where defined, these roles are less supported by the health care system [9,10].

The growing evidence [11,12] corroborates that CPs' extended role beyond traditional dispensing is associated with optimisation of antimicrobial use in primary care. A systematic review and meta-analysis in 2019 [13] demonstrated that a GP-CP team-based implementation of AMS strategies such as group meetings, delayed prescribing, audit-feedback, education and workshop are effective to improve the quality of antibiotic prescribing by GPs. When CPs' AMS roles are guided by policies that support GP-CP practice agreements and patient referrals, the implementation of using point-of-care tests [14,15] and patient-facing leaflet [16] by CPs was feasible and those interventions independently produced substantial effect in reducing inappropriate antimicrobial use and improving patient outcomes.

Though AMS literature in the context of general practice and community pharmacy is growing, AMS research in the GP-pharmacy interface remains scant. To date, there is no AMS model framework elsewhere that guides how GPs and CPs can better engage and collaborate with antimicrobial use. The primary care AMS implementation frameworks which exist are limited to general practice [17] and specific to clinical infections [18]. In Australia, there are GP-CP collaborative care models [19, 20] that support chronic care in primary care, but no such collaborative model incorporates or drives AMS activities. This study aims to develop a general practitioner-pharmacist antimicrobial stewardship (GPPAS) model in Australian primary care by using formative research determining an effective GP-CP collaborative AMS strategies, evidence practice gaps in collaborative AMS practices, and challenges and opportunities of GPs and CPs to collaboratively optimise antimicrobial use.

2. Results

Table 1. summarises the key outcomes and key message of the seven individual studies stepwise explored. Guided by the SEIPS2.0 model, **Table 2** has summarised the key problems, facilitators, opportunities and quality improvement strategies for Australian GPs and CPs to rigorously involve and collaborate in AMS activities. The quality improvement strategies have been fitted into a GPPAS model as key components. The Australian pilot study [26] of a GPPAS sub-model conducted in a general practice found that GP educational intervention facilitated by a team of physician and pharmacist was significantly effective in improving appropriateness in antimicrobial selection (73.9% vs 92.8%, RR = 1.26; 95% CI = 1.18–1.34), duration (53.1% vs 87.7%, RR = 1.65; 95% CI = 1.49–1.83) and guideline compliance (42.2% vs 58.5%, RR = 1.39, 95% CI = 1.19–1.61).

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Table 1. Summary of key findings from seven individual studies which contributes to the development of the GPPAS model.

Studies informed GPPAS model	Methods	No. of studies/Participants (Settings)	Aim	Key Outcomes	Key message
Study 1: Effectiveness of interventions involving pharmacists on antibiotic prescribing by general practitioners: a systematic review and meta-analysis **[13]**	Systematic Review and meta-analysis	35 studies General Practice	To identify whether and what interventions involving pharmacists can improve antibiotic prescribing by GPs.	A meta-analysis of 15 studies found reductions of antibiotic prescribing rate (Odds Ratio 0.86 and 95% CI 0.78–0.95), and improvement of guideline adherent antibiotic prescribing rate (Odds Ratio 1.96 and 95% CI 1.56–2.45) when interventions were implemented by a GP-pharmacist team. A list of effective GPPAS strategies includes: 1) GP-pharmacist group meetings, 2) academic detailing by a GP-pharmacist team, 3) GP-pharmacist collaborative development and uses of local antibiotic guideline, 4) auditing antibiotic prescription and providing feedback to GPs, 5) implementing delayed prescribing strategy by a GP-pharmacist partnership, 6) workshop training involving GPs and pharmacist, 7) use of point-of-care tests in a GP-pharmacist practice agreement model, 8) reviewing of antimicrobial prescription by pharmacist and communication with GPs, and 9) use of common patient education leaflets and antibiotic checklists.	GPPAS interventions were effective to reduce antibiotic prescribing and improve guideline-adherent antibiotic prescribing by GPs. However, context specific evidence is required to understand their usage in routine practice and implementation barriers.
Study 2: Knowledge, perceptions and practices of community pharmacists towards antimicrobial stewardship: a systematic scoping review of survey studies [21].	Scoping Review	10 studies Community pharmacy	To review AMS survey studies and determine the knowledge, attitudes, and practices of community pharmacists regarding AMS.	This review identified that there exists a small (10 surveys globally) but growing body of literature concerning CP-AMS. The dearth of surveys (only three were validated surveys) indicated suboptimal progress of AMS implementation in the community pharmacy. This study findings informed and guided the development of nationwide survey study to comprehensively understand AMS situation in Australian community pharmacy including current challenges.	There are limited number of good quality validated AMS survey instruments around the world to assess CPs' knowledge, use of evidence-based AMS strategies, collaboration with prescribers to identify stewardship targets and monitor stewardship progress in community pharmacy. The mechanism on how to improve engagement of CPs in AMS needs more research in future.

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				Most of surveyed CPs believed that AMS improved patient care (median 86.0%, n = 6 studies), and reduced inappropriate antibiotic use (median 84.0%, n = 2). Half of the participant CPs had some kind of communications with prescribers about the infection control and uncertain antibiotic treatment. Also, nearly half of CPs educated patients. Lack of training, guidelines, access to prescribers, and reimbursement models were majorly reported barriers to AMS implementation by CPs.	
Study 3: A Nationwide Survey of Australian General Practitioners on Antimicrobial Stewardship: Awareness, Uptake, Collaboration with Pharmacists and Improvement Strategies[22].	Nationwide Survey	386 GPs General practice	To assess GPs' awareness of AMS, uptake of AMS strategies, attitudes towards GP–pharmacist collaboration in AMS, and perceived challenges of doing AMS activities in routine practices	Most of GPs were familiar with AMS. Two strategies were found to had increased uptake: use of Therapeutic Guidelines "Antibiotics" (83%) and delayed prescribing (72.2%). The point-of-care tests (18.4%), patient information leaflets (20.2%), peer-prescribing reports (15.5%) and audit and feedback (9.8%) were rarely used. The half of GPs were receptive to the recommendations by pharmacists on choice of antimicrobial and 63% on dose. A policy fostering increased GP–pharmacist collaboration in AMS was supported by more than 60% of surveyed GPs. Patient's desire for a quick-recovery, broad-recommendations of guideline recommendations and access to ID physicians, pharmacists and microbiological services, and a lack of education and training on AMS programs.	GPs are aware of AMS but the uptake of evidence-based AMS strategies are inadequate. Majority of GPs were receptive to a pharmacist's interventions to optimise antimicrobial use. Development of a feasible GP–pharmacist collaborative AMS implementation model, supplying stewardship resources and facilitating training could improve GPs' participation to foster AMS activities in primary care.
Study 4: Antimicrobial stewardship by Australian community pharmacists: Uptake, collaboration, challenges, and needs [23].	Nationwide Survey	613 community pharmacists (CPs) Community Pharmacy	To assess CPs' awareness, uptake of evidence-based AMS strategies, attitudes toward collaboration with GPs in AMS, and	Though CPs were familiar but felt necessity of training (76.5%) and access to AMS practice guidelines (93.6%). CPs often counseled patients and reviewed drug interactions (93.8%) but less frequently used the national Therapeutic Guideline (Antibiotic) (45.5%) and assessed guideline-compliance of prescribed antimicrobials (37.9%). CPs	CPs are aware of the judicious use of antimicrobials but they need training and resources to routinely practice AMS. The receptiveness of GPs and GP-CP collaboration system structure may accelerate CPs' engagement in AMS.

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			barriers to improve AMS practices in pharmacy.	inadequately communicated with GPs (41.8%) regarding suboptimal antimicrobial prescription. CPs believed that GPs are non-receptive to their recommendations. CPs strongly believed that GPs should accept their recommendations on choice (82.6%) and dosage (68.6%). CPs uncommonly used the point-of care tests (19.1%) and patient information leaflets (24.5%). Most surveyed CPs strongly supported policies regarding GP-pharmacist collaboration (92.4%), limiting accessibility of specific antimicrobials (74.4%), and reducing repeat dispensing of antimicrobial (74.2%). The interpersonal, interactional, structural, and resource-level were perceived barriers for CPs to spontaneously participate in AMS activities.	
Study 5: Divergent and Convergent Attitudes and Views of General Practitioners and Community Pharmacists to Collaboratively Implement Antimicrobial Stewardship Programs in Australia: A Nationwide Study [24]	Nationwide Survey	999 Participants Quantitative responses: 386 GPs and 613 CPs Qualitative responses: 221 GPs and 592 CPs General practice and community pharmacy	To unveil GPs' and CPs' convergent and divergent attitudes regarding implementation of AMS and to understand challenges of collaboration in AMS issues between GPs and CPs	The need of AMS training by CPs was significantly higher than GPs ($p < 0.0001$). GPs used Therapeutic Guideline (Antibiotic) at much higher rate than CPs ($p < 0.0001$). No interprofessional difference was found in using patient information leaflets and point-of-care tests. CPs were highly likely to collaborate with GPs ($p < 0.0001$) but both professionals believed that policies that support GP–CP collaboration are needed to implement GPPAS intervention strategies. The collaboration challenges in implementing AMS were lied at the level of person, logistics, organisations and policies.	There are opportunities for GP-CP collaboration in AMS, however, health system structure supporting routine collaboration and collaborative practice agreements between GP and pharmacy practices are key to foster GP-CP interprofessional trust for doing AMS, develop AMS competencies together, and do communications for AMS activities.
Study 6: Systems thinking approach to improve antimicrobial stewardship in primary care[25].	Rapid Review	General practice and community pharmacy context	To analyse system thinking approaches how to improve implementation of AMS in primary care involving interprofessio	Systems thinking could help scrutinise the priority thoughts before, during and after designing and implementing AMS programs in primary care. Important areas involve how to incorporate AMS resources into existing health system and by whom, understanding system structures and external factors that may operationalise AMS	There is an importance of systems thinking to figure out the optimal arrangement of AMS resources, their access to health professionals, system structures supporting routine AMS activities, dynamic system behaviors, and interprofessional communication and collaboration for designing and implementing AMS programs in primary care

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			nal collaboration and communicatio n	programs, building interdependent AMS team and predicting change of antimicrobial use over time. Opportunities are surmounting regarding how to transform antimicrobial use behaviours culturally and structurally through establishing sustainable AMS friendly health service model that ensures patient centred but interprofessional antimicrobial care in primary care in future.	
Study 7: The effectiveness of a simple antimicrobial stewardship intervention in general practice in Australia: a pilot study [26].	Pilot implementati on study in Australian primary care	A General Practice in Victoria, Australia	To evaluate the impact of a novel GP educational intervention involving pharmacists improving appropriatene ss and guideline compliance of antimicrobial prescriptions	GP education AMS program was significantly effective in improving appropriateness in antimicrobial selection (73.9% vs 92.8%, RR = 1.26; 95% CI = 1.18–1.34), duration (53.1% vs 87.7%, RR = 1.65; 95% CI = 1.49–1.83) and guideline compliance (42.2% vs 58.5%, RR = 1.39, 95% CI = 1.19–1.61).	The implementation of a GP education program involving pharmacist is effective to significantly improve appropriateness and guideline compliance of GPs' antimicrobial prescription. The findings indicate that GP-pharmacist AMS education model has an important role and should be sustainably continued for antimicrobial education within general practice.

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Table 2. Synthesised summary evidence regarding the key problems, facilitators, opportunities and quality improvement strategies for Australian GPs and CPs to rigorously involve, collaborate and routinely implement AMS activities that inform the design of the GPPAS model framework.

Key problems	Facilitator	Opportunities	SEIPS component	Proposed quality improvement strategies
Limited education, training and professional development regarding AMS practice, strategies and goals	The implementation of AMS training courses as part of the professional development modules of GPs and CPs are essential for their competency in AMS and participation in collaborative AMS activities. Incorporation of these courses into the GP/pharmacy curriculum of undergraduate and graduate program would be valuable.	GPs (46.4% of 386) and CPs (76.5% of 613) felt that they would need AMS education and training. Most GPs (72% of 386) and CPs (87.3% of 606) strongly agreed to receive AMS training in future.	Person	**AMS education model**
Potentially limited resources for use to make a shared decision about antimicrobial use during consultation and counselling with a patient	Antibiotic checklist, AWaRe tools, and patient-facing information leaflets.	Less than 25% of surveyed GPs and CPs used patient information leaflets.	Physical Environment Tools and Technology	**Access to AMS resources**
Patient expectation to get antimicrobial prescription while visiting a GP/CP with a symptom non-suggestive of antimicrobial use	Patient education and antimicrobial awareness campaign. Provide a patient a take-home message about how to self-care and seek further advice in treating self-limiting infections.	Most GPs (76.8% of 383) and CPs (82.4% of 608) educated patients about unintended consequences of antimicrobial use (e.g., AMR, gut effect) but without using any formal tools.	Person Task	**GP-patient communication** **CP-patient communication**
Lack of GP-CP communication regarding antimicrobial prescription	Receptiveness of GPs to accept CPs' recommendations Information technology support, Telehealth-led antimicrobial reviews, case conferencing.	GPs felt that they should be receptive to CPs' recommendations on the choice (50.5% of 381) and dose (63% of 382) of antimicrobials.	Person Organisation Tools and Technology	**Interprofessional AMS education model** **Health system structure**
No local or national GP-pharmacy practice agreements and policies supporting collaboration in AMS	GP-CP practice agreements and relevant policies	Most CPs (94% of 606) and majority of GPs (60.9% of 381) believed that a policy supporting their collaboration in AMS is needed to improve AMS in the community	Organisation External Environment	**Policy environment**
Poor tracking and monitoring system to identify inappropriate prescribing and provide feedback	Validated tools supporting antimicrobial audits GP-pharmacist local AMS team	GP-pharmacist collaborative antimicrobial audit- model were inter-professionally (46.1% of GPs and 86.5% of CPs) supported to optimise antimicrobial therapy	Organisation	**GP-pharmacist audit feedback model**
CPs' lack of access to clinical indications and diagnostic reports to review antimicrobial prescription	User friendly "MY Health Records", GPs' mandatory reporting of clinical indication for antimicrobial prescription	Most CPs believed that having access to a patient's clinical and diagnostic information would assist reviewing the guideline-adherence of prescribed antimicrobial(s)	Physical Environment	**GP-pharmacist antimicrobial review model** **Access to AMS resources**

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				Health system structure
Lack of technology support to take optimal decision about antimicrobials during busy practice environment.	CDSS, eTG (Antibiotic) integrated with prescribing and dispensing software	Nearly 30% of surveyed GPs and CPs felt that AMS resources linked to prescribing and dispensing software will help them to consider AMS in a busy environment	Tools and technology	**Health system structure**
Diagnostic uncertainty about the cause of infections	Availability and accessibility of point-of care tests in GP and pharmacy facilities	Less than 20% of surveyed GPs (N=386) and CPs (N=613) used point of care tests	Tools and technology	**GP-pharmacist diagnostic stewardship model**

2.1. Description, operationalisation and implications of the GPPAS model

Using our studies and international evidence, we propose a theory and evidence-informed GPPAS implementation model framework (**Figure 1**) which consists of seven interactive domains under work-system that demonstrates how AMS can rigorously be implemented in Australian primary care by fostered patient centeredness and GP-pharmacist collaboration. Seven interactive domains include: 1) pharmacist-patient, 2) GP-patient, 3) GP-pharmacist, 4) resource access (tools and technology), 5) organisational structure 6) task and 7) policy environment to foster interpersonal and interprofessional collaboration in AMS. The GP-pharmacist domain of the GPPAS model composed of five evidence-based GP-pharmacist team based sub-models for routine AMS implementation: interprofessional AMS education, antimicrobial audits, diagnostic stewardship, delayed prescribing by GP-pharmacy partnership, and routine antimicrobial prescription review models. Implementation of these sub-models would foster collective participation and collaboration of GPs and CPs. Overall, improving AMS work system would change cognitive and social behaviours at patient, professional and practice level to achieve the desired outcomes of optimal antimicrobial use, reduced patient harms with unnecessary antibiotic use and reduced risk of growing antimicrobial resistance in primary care.

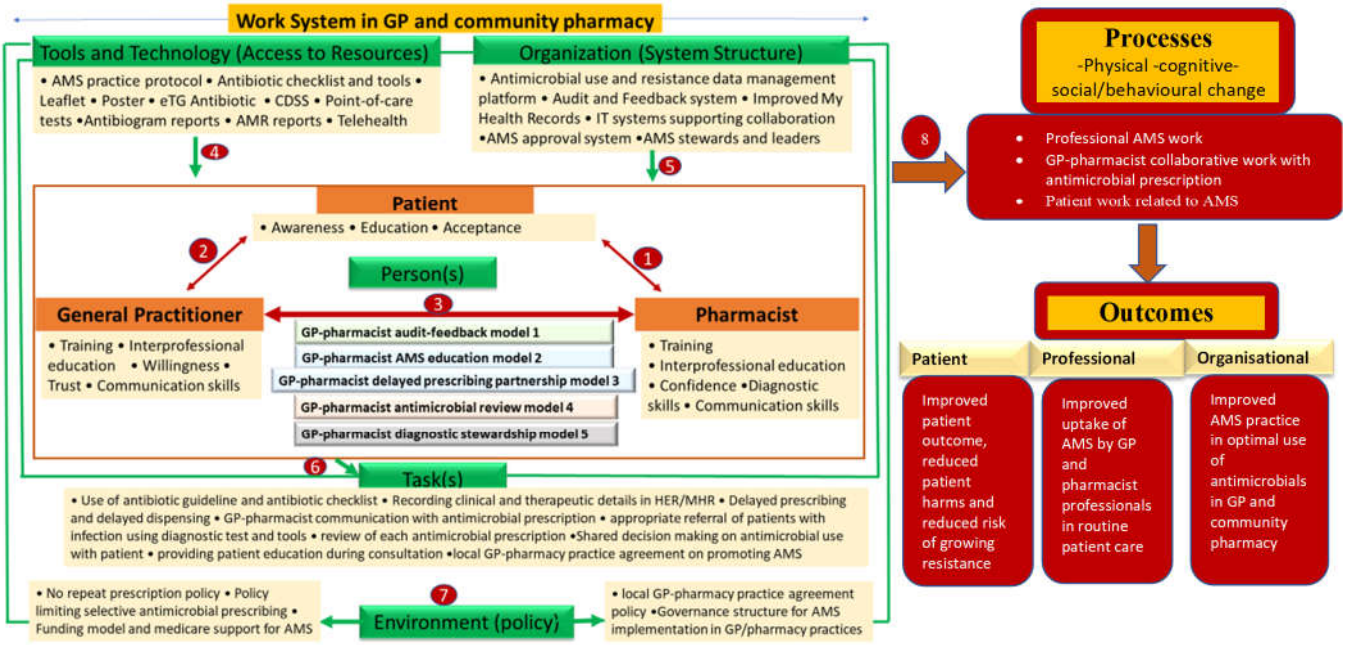

Figure 1. GPPAS Model guiding AMS implementation by fostered GP-pharmacist collaboration. [eTG: eletronic Therapeutic Guideline; CDSS: Clinical Decision Support System; IT: Information technology; MHR: My Health Record; EMR: Eletronic Medical Record; AMR: Antimicrobial Resistance; AMS: Antimicrobial Stewardship; GPPAS: General Practitioner-Pharmacist Antimicrobial Stewardship].

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2.2. Pharmacist-patient

Community pharmacy is the first point of contact for most patients who seek care or advice from a pharmacist for treating minor ailments or self-limiting infection(s). Furthermore, CPs are the most accessible source for patients to get antimicrobial(s). Pharmacist-patient interactive communications thus can play an important role in educating patients about how to prevent minor infections without antimicrobial(s) and safe use of antimicrobial(s). As guided by SEIPS 2.0 model, an interpersonal trust and dependency between a CP and a patient is critical to improve a patient's desired antimicrobial use behaviours by impacting their individual knowledge, motivation to act, and changing social norms for safe antimicrobial use in primary care.

Our GPPAS model emphasises that upon a patient's visit to a pharmacy, a CP should play some essential roles which are also supported by literature [27-34]: i) diagnostic assessment of infections to an extent to appropriately identify a patient's needs (e.g., OTC, antimicrobial, referral to GPs), ii) patient education where possible about the self-limiting infections, completion of full course of antimicrobial therapy as prescribed, avoiding the use of left-over antimicrobial(s), and effect of antimicrobial use on the gut, and iii) asking patient to call a pharmacist if any allergies or side effects occur during the period of antimicrobial use and iv) giving instruction to patients about their return of left-over antibiotics to pharmacists.

Supplementary table 1 shows evidence [16, 35-37] of effectiveness in support of using those resources by CPs to influence patient referral to GPs, and patient knowledge, antibiotic seeking behaviours and antibiotic consumption. Australian CPs face significant challenges in the availability and use of patient education and diagnostic resources in routine patient care and most CPs provide patient education about antimicrobial(s) and resistance but without using any formal communication tools as reflected in our study.[31]

2.3. GP-patient

The GPPAS model stresses a GP-patient interactive communication as important as CP-patient interaction as a joint effort to identify patient concern and reduce patient pressure on antibiotic decisions during consultation and impact patient awareness on prudent use of antibiotics in long run. In support of this domain, international literature evidence [17, 38-41] has been reported in supplementary table 1.

2.4. GP-pharmacist

An inter-disciplinary approach [42-44] is a key to effectively implement AMS programs. Our study evidence proposes five intervention-focused implementable models under the GP-pharmacist domain of the GPPAS model: GP-pharmacist audit-feedback model, GP-pharmacist AMS education model, GP-pharmacist partnership based delayed antimicrobial prescribing model, GP-pharmacist antimicrobial review model, and GP-pharmacist diagnostic stewardship model.

2.5. GP-pharmacist audit-feedback model

Antimicrobial audit and feedback model is a proven, effective, and sustainable model [13, 45] where GPs and CPs need greater involvement to improve the quality of antimicrobial use. As our studies [22, 23] found, both GPs and CPs demonstrated positive attitudes towards interprofessional involvement in antimicrobial audits. Though auditing antimicrobial prescription is common in Australian hospital settings, resources and structural set up to drive audits in primary care are potentially limited and underdeveloped: quality indicators for the optimal use of antimicrobials; electronic databases that facilitate clinical and antimicrobial audits; a dedicated interprofessional team; and context-specific tools to audit antimicrobial prescriptions. Developments in those areas could help pharmacists to be more engaged in regular antimicrobial audits, reviewing stewardship indicators and related communication and feedback to GPs. In Australia, a tool [46] to audit antimicrobial use in the remote primary healthcare has been tested and this tool could be

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integrated into GP practice in future. Considering feasibility of the model, audits and written feedback to GPs could be undertaken for the selective antimicrobial prescription(s) such as prescription for RTIs or UTIs (where antibiotic mis-prescribing is higher) but with a regular interval (e.g., monthly, or quarterly a year). Evidence [47, 48] of such pharmacist led effective audit model in primary care has been shown in Supplementary table 1.

This model suggests that a pharmacist would collaborate with the local AMS team to identify the educational needs, build program initiatives, and plan for data collection, and share and discuss the audit-feedback program outcomes. Sustained funding and involvement of an infectious disease physician, AMS pharmacist and GP opinion leader to support audit programs should be a policy decision. In Australia, few GP clinics where pharmacists are co-located, can be a setting for testing this model as a priori. Implementation feasibility of this model would need better access of general practice and community pharmacy to an AMS pharmacist or infectious disease physician where possible and relevant education, training and practice protocol for CPs.

2.6. GP-pharmacist AMS education model

Person-centered AMS training model for GPs and pharmacists

AMS education and training for GPs and CPs have been found essential both in literature [11,17,18, 49-52] and in our baseline evidence [22,23] when it comes to undertaking AMS in routine patient care. Despite AMS training is a core component of AMS programs, training targeting primary care clinicians is limited. Only one-third of our surveyed GPs and CPs in Australia had completed the antimicrobial modules of the NPS Medicine Wise [22,23]. This limited uptake demonstrates the implementation challenges of AMS training among GPs and CPs. Van Katwyk et al [52] identified 94 AMS related educational programs globally but few are accredited training programs. The feasible implementation and sustained impact would have been desirable if those training courses were incorporated and regulated into the graduate curriculum of GPs and CPs [53].

GP-pharmacist interpersonal AMS education model

A platform that may help GPs and CPs to learn AMS from each other's professional perspectives is lacking in Australia. We propose a GPPAS education model that can be defined as the community-based model where GPs and CPs would co-construct AMS knowledge by sharing areas of problematic antimicrobial prescribing decisions, exploring dissonance in opinion, and developing consensus about a safer antimicrobial therapy between themselves. The system development approach and theories of interprofessional education backed up this model. The support and network from AMS physicians and AMS pharmacist are important to newly establish this model in any setting. The proposed model would likely to develop a sustainable interprofessional AMS learning process and platform, and utilise pharmacists' expertise on antimicrobial pharmacotherapy, pharmacokinetics, pharmacodynamics, dosing, antimicrobial spectrum, and resistance to influence GPs' antimicrobial prescribing. Such a model has international evidence [53-56] reported in supplementary table 1. In Australia, GPPAS education model was significantly effective in improving appropriateness in antimicrobial selection (73.9% vs 92.8%, RR = 1.26; 95% CI = 1.18–1.34), duration (53.1% vs 87.7%, RR = 1.65; 95% CI = 1.49–1.83) and guideline compliance (42.2% vs 58.5%, RR = 1.39, 95% CI = 1.19–1.61) [26].

The mode of implementation involves GP-pharmacist regular group meetings and GP-pharmacist co-led workshop training. Study GPs and CPs in Australia have a motivation to be involved in the co-construction of AMS knowledge by collaborative learning processes [24]. A GP–CP collaborative group meetings model was inter-professionally supported (GPs vs. CPs; 54.9% vs. 82.5%) to optimise antimicrobial therapy though there was an attitudinal divergence [24]. This result indicates that GPs should be open enough to inter-professionally share and accept interventions when justified to improve the quality of antimicrobial prescription(s) and to learn as a team. Creating a culture that supports

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to co-construct AMS knowledge is important in order to develop a sustainable interprofessional AMS learning platform in primary care.

To facilitate such interprofessional AMS education programs in Australia, development of a local GP-CP interprofessional team as site champions is a foremost step for implementation. Incorporating this sub-model into existing GP-pharmacist collaboration models such as pharmacist co-located in general practice model [19] and a home medicine review pharmacist model [20] could be worth trying where a growing number of CPs work in collaboration with GPs for patient cohorts with significant concern of polypharmacy. The professional GP (e.g., Royal Australian College of general Practitioners, RACGP) and pharmacy (e.g., Pharmaceutical Society of Australia, PSA) organisations, NPS Medicine Wise, and the Primary Health Network (PHN) have a major role to collectively develop interprofessional AMS education training programs. Future research is needed to understand the practicality of how to execute this model in primary care.

2.7. GP-pharmacist partnership based delayed antimicrobial prescribing model

The delayed antimicrobial prescribing strategy has been proven as an effective AMS approach [57, 58] to impact antimicrobial dispensing rates [59], however, its true effect in the reduction of antimicrobial use by patients remain unclear. This is perhaps due to the fact that GPs may delayed prescribe antimicrobial(s) but CPs might not delayed dispense for some reasons such as a patient's demand or CPs' strong commitment. This raises questions about the implementation process of this strategy. According to our GP-survey study [22], most GPs (72.2% of 385 GPs) frequently used this strategy. Another study [60] with 103 Queenslander CPs in Australia, 40% would dispense a delayed antibiotic prescription within 24 hours of GP visit by a patient and 60% of CPs wouldn't. CPs could play an important role in implementing delayed prescribing strategy, but they are still under-used resources in Australia. We propose a local GP-CP partnership model to foster implementation of a delayed prescribing strategy and to harness the involvement of CPs in the strategic implementation in primary care.

2.8. GP-pharmacist routine antimicrobial review model

Routine review of antimicrobial prescription is a useful patient-centric approach to optimise antimicrobial therapy. The routine review thus has become an important part of the AMS activities by pharmacist because of identifying many aspects of prescribing compared to passive antimicrobial audit model. CPs' review of GPs' each antimicrobial prescription model is likely to provide an active learning and teaching opportunities for CPs and GPs for routine AMS. A key advantage of this model is that each antimicrobial prescription can be assessed for patient safety, AMR risk and cost savings.

General medication review happens in community pharmacy, however, related training and a checklist that would guide CPs about when, what, and how to commence reviewing antimicrobial prescription are not readily available. This might be one of the reasons why CPs less often assess guideline-adherence of antimicrobial prescription and less likely communicate with GPs when the choice of an antimicrobial is believed to be suboptimal. Our study found that more than 40% of CPs didn't feel confident to assess guideline-adherence of prescribed antimicrobial(s). This post prescription review role of CPs should be a part of routine pharmacy practice to avoid antimicrobial medication errors and ensure guideline-compliance. Advocating these essential roles of CPs could create scope to produce AMS pharmacist stewards, support CPs to develop AMS skills and eventually sustainably reduce some problematic prescribing. Using a GP-CP team-based routine antimicrobial prescription review model would be one of the approaches that need future development and evaluation.

Pragmatically, antimicrobial review can be specific to infections or patient categories, or type of antimicrobial prescribed (e.g., broad-spectrum). Access to a patient's clinical indication and diagnostic reports including antibiogram would be important to facilitate this model. For CPs who work as a home medicine review pharmacist and co-located

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pharmacist in general practice, testing this model in those settings might be practical step forward. CPs role of antimicrobial review has been supported by international literature (supplementary table 1) [11, 32-34, 61].

2.9. GP-pharmacist diagnostic stewardship model

Diagnostic uncertainty is one of the most cited reasons of the inappropriate use of antimicrobials in the community [62-64]. Practically, it is often a challenge for GPs and CPs to differentiate between bacterial and viral infection(s) based on apparent clinical symptoms. Diagnostic uncertainty causes GPs to unnecessarily prescribe an antimicrobial for infections that are treatable without antimicrobial and GPs to err on the side of caution [65]. Similarly, due to diagnostic uncertainty a CP inappropriately and unnecessarily refers patients to GPs, increasing the risk of a patient having an antimicrobial prescription and/or dispense antimicrobial(s) when it is not warranted. We propose a GP-CP collaborative diagnostic stewardship model in Australia to minimise unnecessary use of antimicrobials caused by diagnostic uncertainty. Supplementary table 1 describes evidence and use of these test at international context [7, 14, 66-71].

The uptake of point-of-care tests by the Australian GPs and CPs was below 20% as found in our 2019 nationwide surveys. The evidence indicates that an improved patient referral system, collaborative practice agreements and user training would help to introduce a new GP-CP collaborative diagnostic stewardship model in Australia. This model would have implications to i) increase two-way appropriate patient referrals from and to GPs and CPs; ii) make sure whether a patient needs either antibiotics or over the counter (OTC) or GPs/CPs-visits to optimally treat infections. The provision of this model could improve the scope of CPs to be better involved in AMS programs and optimise infectious disease patient care in community pharmacy.

2.10. Tools and technology (Access to resources)

The active involvement of GPs and CPs in AMS programs and implementation of GPPAS strategies require relevant resources, tools and technologies; clinical decision support system, prescribing and dispensing software integrated with updated antibiotic guideline, regional antibiograms and AMR reports, "My Health Records" providing sufficient clinical and medication information for review by pharmacists, point-of-care tests facilities, WHO AwaRe antibiotic tools, patient-facing information leaflets and a checklist defining GP-pharmacist interprofessional activities in AMS. These resources will increase awareness, motivation and confidence of GPs and CPs to effectively conduct routine AMS tasks. For instance, the use of patient-facing leaflets is an opportunity for both GPs and CPs to provide safety netting advice to patients, revise the decision of antimicrobial use and address demands for antimicrobials by patients.

2.11. Organisation (System structures)

An organisational support has been deemed as important to set up a GPPAS model in routine patient care and to support GPs and CPs to collaborate with antimicrobial prescription(s). The GP/pharmacy organisational initiatives which have been found as priorities to facilitate implementation of evidence based GPPAS strategies include: i) development of antimicrobial use and resistance data sharing platform between GPs and CPs, ii) building a local GP-CP network for collaboration iii) pharmacists' access to a patient's health records including antimicrobial prescription iv) general practice-community pharmacy practice agreements for AMS, v) interprofessional organisational structure that ease patient referrals and enable patient follow up by GPs and CPs who are on antimicrobials and vi) organisational support for GP-CP collaboration in AMS. There are structural limitations to routinely monitor appropriateness of prescribed antimicrobial(s), patients' clinical and therapeutic outcomes and provide feedback to GPs. Implementation of a GP-pharmacist antimicrobial audit and feedback model and routine antimicrobial prescription review model thus need a sustainable data solution. The SEIPS 2.0 model component,

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"tools and technology" guides that these data should fit into the workflow of GPs and CPs.

2.12. Task

The GP-CP collaborative routine task as shown in the figure would foster implementation of AMS. All other interconnected domains of the GPPAS model would facilitate these tasks according to SEIPS 2.0 model.

2.13. Policy environment

Having a national governance structure for implementing AMS programs in primary care is a policy priority. GP and pharmacy representatives in the governance structure would determine and provide a strategic direction to foster GP-CP collaboration in AMS. The external environment such as GP/pharmacy AMS practice guidelines and protocols may drive implementation. The adoption of societal norms and policy on restricted use of broad-spectrum antimicrobials, stopping repeat prescriptions, establishing GP-pharmacy practice agreements and d) incentives and/or medicare support for local GP-CP collaboration in antimicrobial prescription and infectious disease management programs could influence AMS progress in primary care. These societal interventions and policies need greater attention by AMS stakeholders to support implementation of GPPAS model in primary care. The Australian national regulatory framework for RACGP accreditation and the national competency standards framework for pharmacists in Australia should incorporate AMS programs involving GP-CP collaboration as an accreditation criterion to foster implementation of AMS in primary care.

2.14. Process and outcomes

According to the SEIPS theoretical model if a work system (**Figure 2**) has been set up in GP and pharmacy practices, the professional AMS activities and collaboration will be accelerated through cognitive, social and behavioural changes among GPs and CPs. This process would influence in achieving desired outcomes: improving uptake of evidence-based AMS strategies by GP and CPs; optimising the use of antimicrobials; improving patient outcomes; and reducing patient harms and resistance.

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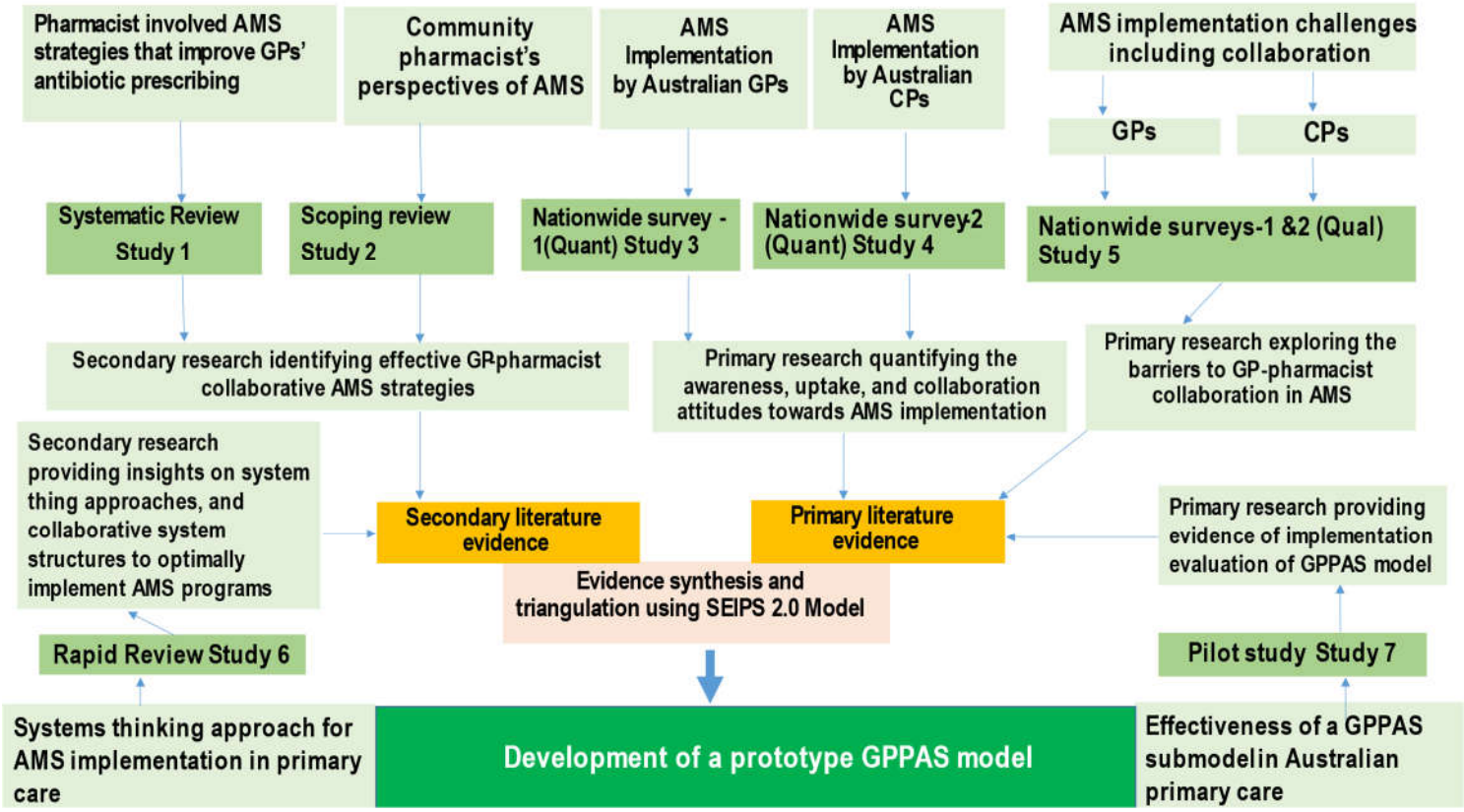

Figure 2. Stepwise development of the GPPAS model.

3. Discussion

Compared to hospital settings, the implementation of AMS programs in primary care is potentially limited though most antimicrobials are used in primary care. Acknowledging that primary care practices are everchanging, diverse and influenced by a lack of interprofessional health service models, it is imperative to develop a sustainable AMS implementation model involving GP-pharmacist collaboration in primary care. Unlike hospitals, primary care GPs and pharmacists often provide infectious disease patient care with or without antimicrobial(s) independently and with bare communication and collaboration. This independent practice and organisational business models are non-supportive of a team-based patient care which makes AMS implementation challenging. The national GP and pharmacy organisations, and AMS implementation bodies must come to the realisation that this missing connection between GPs and pharmacists leads sharp rise of inappropriate antimicrobial use and increase the burden of AMR in primary care. Establishment of an AMS implementation framework involving GP- pharmacist collaboration is thus a fundamental health system improvement approach to respond to the burden of AMR in primary care. To our knowledge, no such implementation model exists in current literature except few AMS models [17,18] specific to GP practice and management of respiratory tract infections in primary care.

Our study for the first time has added new knowledge in an under-researched area of GP-pharmacist collaboration in AMS. We provide important insights into how Australian GPs and CPs could be better engaged in AMS and present a theory informed and evidence based novel GPPAS implementation model framework. Each component of the GPPAS model has been explained using Australian and international evidence as demonstrated in the model description and supplementary table 1.

A GPPAS sub-model was well received, cost effective and showed potential for improving appropriateness and guideline compliance of antimicrobial prescribing by GPs in Australia [26]. Whether and how long these improvements sustained after ceasing GPPAS intervention is also worth exploring. Such a study has been done and will be shortly

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published by our research team elsewhere. Other sub-models also need future assessment to predict the overall effectiveness of the GPPAS model.

The study has some drawbacks. Methodologically, an indepth qualitative study (e.g., paired interviews) and multi-centered pilot study would also have been ideal to refine the model components and to inform future randomised controlled trials. However, those studies were out of scope of the PhD project. Though SEIPS 2.0 model established theories for the GPPAS model, other frameworks such as theoretical domain framework [72] and implementation science theory [73] might have been used as alternative approach to make this model work in real life because of the complex nature of AMS interventions and diverse primary care practices. The detailed limitations of the seven formative studies that inform the GPPAS implementation model has been explained in our previously published literature [13, 21-26].

Future research is needed for the refinement of the GPPAS model by co-design approach and implementation evaluation by clinical trials and qualitative study using grounded theory or behavioural approaches [74-76]. Lastly, our GPPAS implementation model could be utilised as a guide for stakeholders and policymakers to design and implement AMS program utilising GP-pharmacy collaboration in primary care both nationally and internationally. The model could have significant policy implications to define, involve and foster the much-required role of CPs in the implementation of AMS programs at national and international context.

4. Conclusion

A GPPAS model has been successfully designed which will guide and accelerate the implementation of evidence-based AMS programs by improved GP-pharmacy collaboration in Australian primary care. The model could have significant policy implications to foster GP-CP collaboration in AMS. Future implementation trials are needed to deeply understand the feasibility and cost effectiveness of the GPPAS model for national scalability to sustainably optimise antimicrobial use in primary care.

5. Methods

This was an exploratory study framed with a systematic review, a scoping review, nationwide surveys including qualitative components, a rapid review and a pilot study to inform a prototype GPPAS implementation model. The overarching project collecting secondary and primary evidence was conducted between 2017 and 2021. Saha et al 2021[77] detailed the methodologies that guide the development of the GPPAS model. Systematic review [13] were undertaken to identify and describe the list of effective GPPAS interventions and model components using Template for Intervention development and reporting (TIDIeR) checklist. AMS surveys of GPs and CPs across Australia were designed to explore the convergent and divergent views of GPs and CPs about the GPPAS interventions, attitudes towards collaboration in AMS and the perceived challenges of implementing GPPAS interventions. A pilot study in an Australian general practice [26] determined the effectiveness of a GPPAS submodel. Synthesised evidence from all studies informed the prototype GPPAS model framework. **Figure 2** diagrammatically show how seven studies inform the development of the GPPAS model framework.

5.1. Theoretical model selection

The theory and evidence-based approaches were employed to develop a GPPAS model. We identified the Systems Engineering Initiative in Patient Safety (SEIPS 2.0) model [78] as a vehicle for translating our results into a model that would guide how to foster AMS implementation in primary care by GP-CP collaboration. The SEIPS 2.0 model guided the theoretical structure of the GPPAS model through identifying the determinants of GPPAS uptake, and barriers and facilitators to implementing AMS by GP-pharmacist collaboration.

Human factors engineering is the scientific approach to understand interactions among humans and elemental part of a system [79]. The SEIPS 2.0 model is one of the leading frameworks in the discipline of human factor engineering research [78]. According to the SEIPS 2.0 model, the workplace (e.g., GP clinic or community pharmacy) characteristics and work system do interact spontaneously. This model identifies the problems in a work system that consists of person(s), tools and technologies, organisation, tasks, and the physical environment within a wider societal environment. The work system influences the processes or practices by health professionals (e.g., GPs or pharmacists) such as prescribing practices and dispensing practices of antimicrobials, that influence outcomes of patients with infection(s) and impacts on AMR.

The application of the SEIPS2.0 model is rising to improve the safety of patients and the quality of care in various health care settings [79-83]: more than fifty studies have used the model for assessing the safety of patients in health care, ranging from hospital to primary care clinics. Importantly, the SEIPS model has ability to evaluate the causes of medical errors and the process of how to control it [78]. Hence, this model is a natural fit for delving the behavioural and systematic components of AMS involving general practice-pharmacy collaboration. This model helps to identify interventions at an individual, structural and an environmental level to foster AMS by a GP-pharmacist collaboration. The SEIPS 2.0 model therefore determined the building blocks of the GPPAS model.

5.2. Evidence synthesis and analysis

A critical synthesis approach was used to collect evidence from multi-method research [84]. We merged and triangulated evidence derived from our published studies (Table 1) using a SEIPS2.0 theoretical framework. A team of researchers responsible for each individual study summarised the key outcomes for each study: effective GPPAS strategies, commonly and uncommonly used GPPAS strategies, barriers and facilitators to collaboratively implement GPPAS strategies by GPs and CPs, and attitudes towards GP-CP collaboration in AMS. Authors evaluated and compared evidence from multiple literature where possible to weigh the evidence. Evidence from systematic reviews and meta-analysis and evidence from multiple sources were considered as strong evidence. The designed GPPAS model has been described with supportive evidence from multiple sources in the result section. The evidence from a pilot study of a GPPAS model component strengthen the contextual evidence in Australian primary care. Upon triangulation, we identified key model components and drew the structure of the GPPAS model framework. The intervention-based GP-CP collaborative implementation sub-models were then mapped out under the GPPAS model framework. The required resources and policies were identified and proposed to integrate those models into existing GP-pharmacist interprofessional care model in Australia. The amalgamation of synthesised evidence eventually informed a prototype GPPAS implementation model framework.

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