Guidelines, policies and documents supporting AP: the UK landscape

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Background information

- *Anticipatory prescribing (AP) is the prescription and dispensing of injectable medications to a named patient, in advance of clinical need, for administration by suitably trained individuals if symptoms arise in the final days of life.*

- Injectable medications typically prescribed for: **pain** (opioid), **nausea and vomiting** (anti-emetic), **agitation** (midazolam), **respiratory secretions** (anticholinergic)

- UK-wide practice despite limited evidence-base (Bowers et al. 2019). First published report of AP practice in the community in 2005 (Amass, 2005)

- Endorsed by NICE 'Care of dying adults in the last days of life' (NG31), 2015 and a range of other UK policy documents[1, 2]

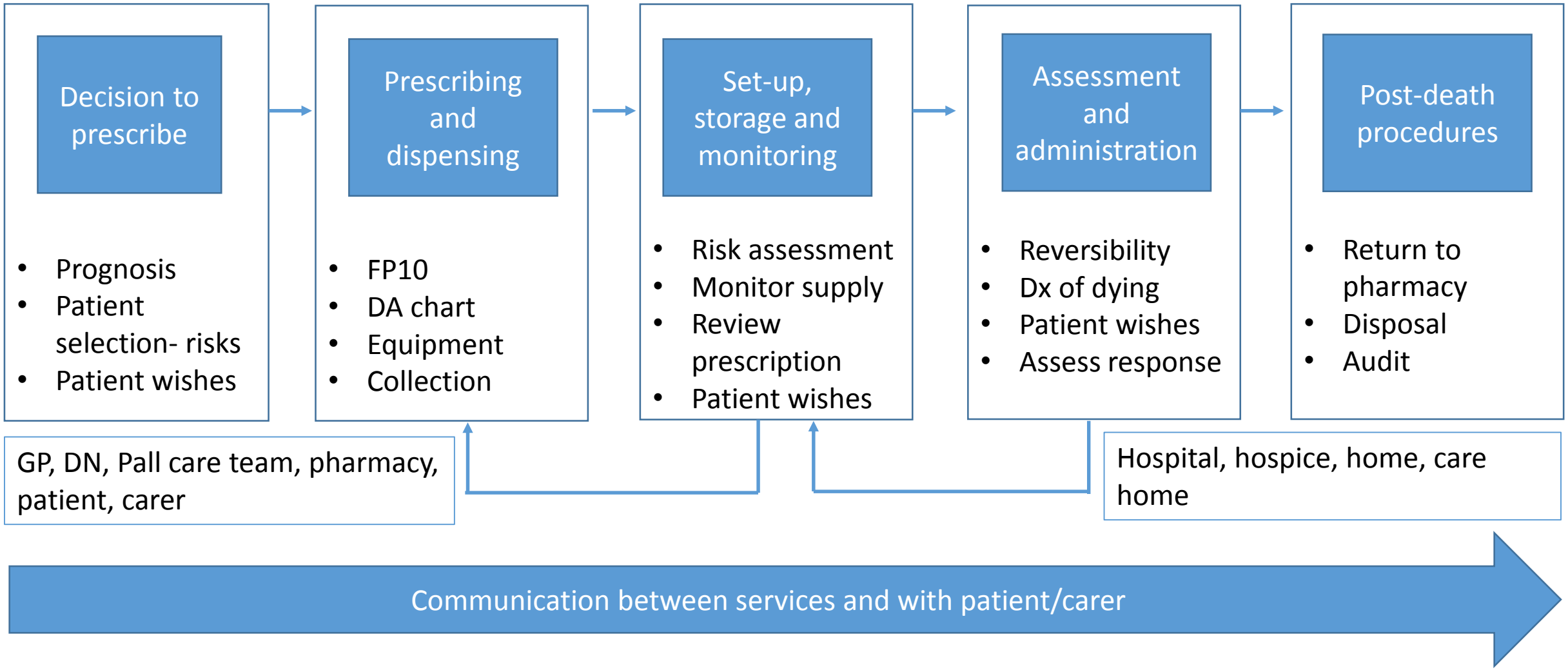
1. DOH(2004) Securing proper access to medicines in the out-of-hours period
2. National End of Life Care Strategy (2008)

A ‘simple’ solution to a complex problem?

Aim	Context
1. *‘to enable rapid relief at whatever time the patient develops symptoms’ (NICE QS144, 2017)*	1. Difficulty accessing medications during OOH period (Thomas, 2001)
2. *to ‘prevent distressing hospital admissions’ (*NG31, 2015)	2. Change in the nature of OOH care: less continuity
	3. More stringent controlled drugs regulations (2007)
	4. NHS financial constraints

K. Thomas (2001). Out of hours palliative care in the community: continuing care for the dying at home
DOH (2000): Raising Standards for Patients: new partnerships in out-of-hours care

A complex intervention in a complex system

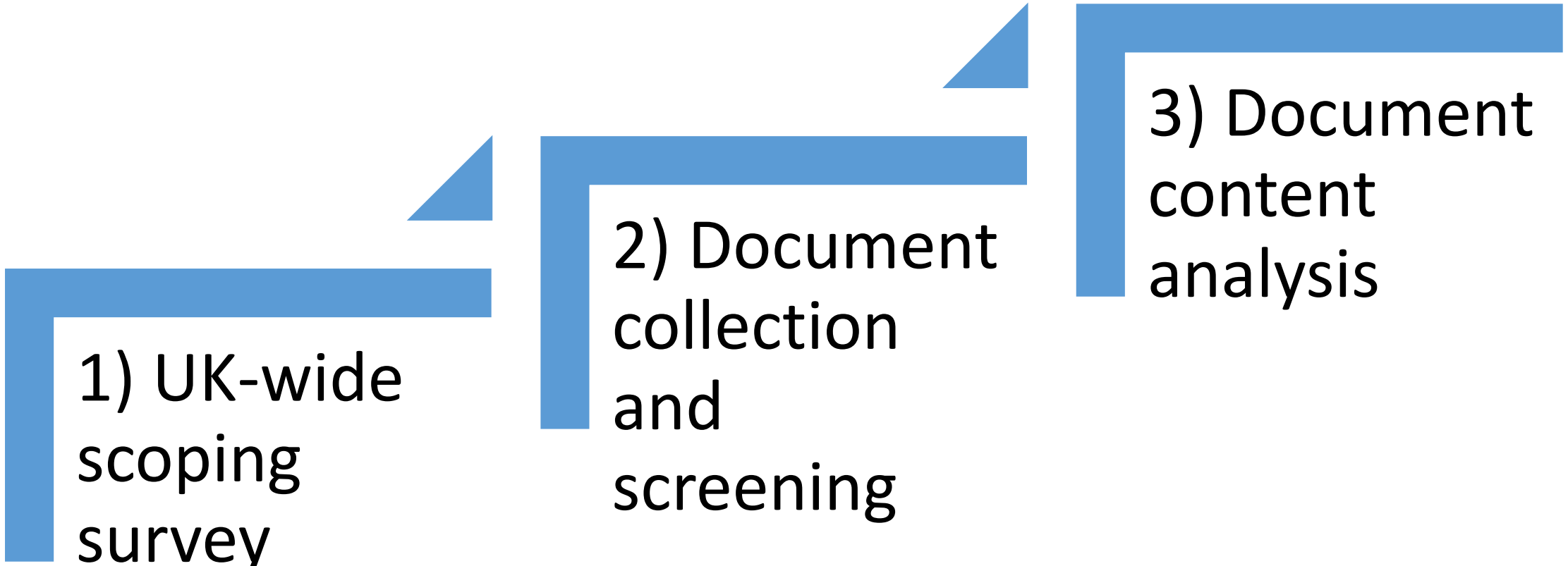


Aim and objectives

- To investigate the role of AP governance documents in guiding anticipatory prescribing practice in community end of life care across the UK.
  - Initially focused on local/regional documents but later expanded the analysis to include national documents

- *How is AP practice governed and facilitated across the UK?*
  - *a) What is the nature and scope of documents governing AP practice?*
  - *b) What is the content of documents governing AP practice?*

Methods overview



1) UK-wide scoping survey- methods

- Survey sent to identified stakeholders (senior EOLC clinicians or commissioners) for each of the following areas:

- England: random stratified sample of 55 CCG areas, stratified by local health region, size, urbanization
- Scotland: all 14 health board areas
- Wales: all 7 health board areas
- Northern Ireland (NI): all 5 local commissioning groups

- Responses analysed at the CCG/local health board level

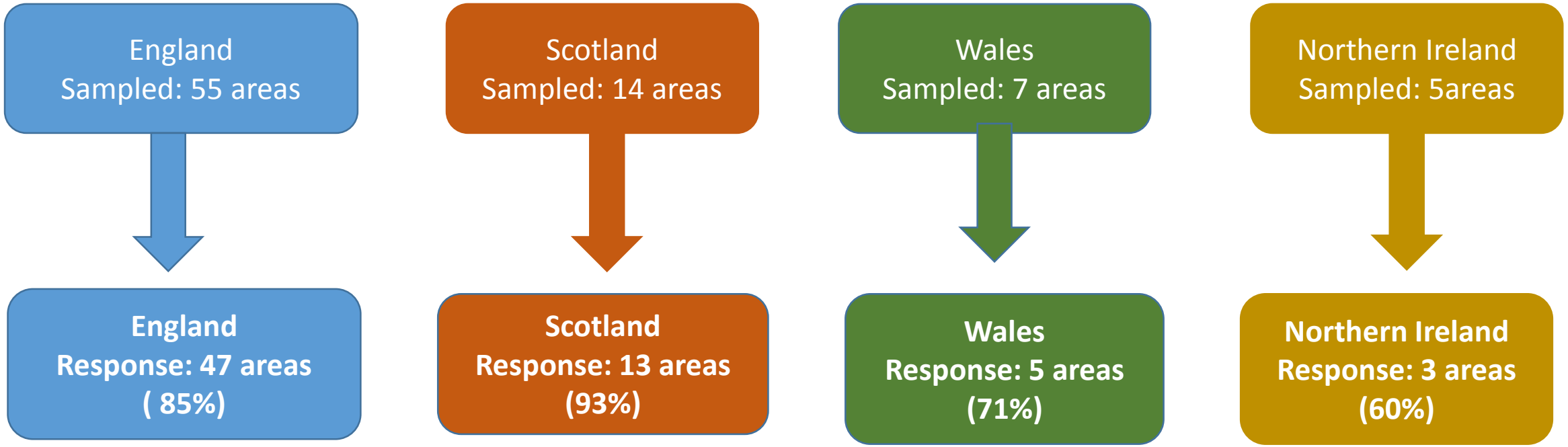
Email survey

What types of documents do you have in place in the (CCG name) area to guide and facilitate anticipatory prescribing at the end of life in the community?

In particular, we would like to know if you have any of the following (please indicate with 'yes' or 'no' if possible):

1. ***Policy (yes/no)***
2. ***Guidance (yes/no)***
3. ***Standard operating procedure (yes/no)***
4. ***Drug authorisation chart (also known as a MAR or community prescription chart) (yes/no)***
5. ***Patient information leaflets (yes/no)***
6. ***Any other supporting documents (yes/no)***

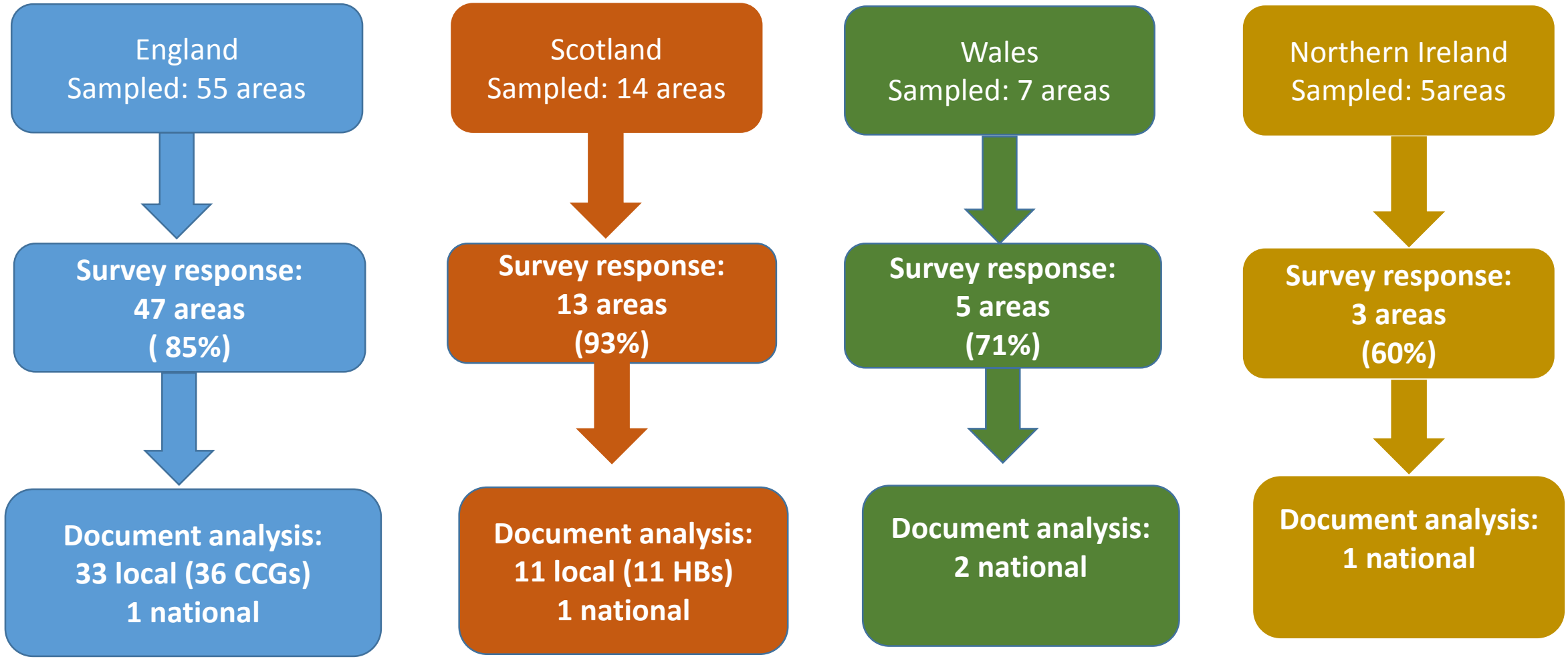
Survey results: CCG/health board area response:



Survey results: the UK landscape

	Governance level	National document	Document types Relationship between national and local documents
England	National and local	NICE Care of Dying Adults in the Last Days of Life (NG31), 2015	• **National:** guideline only • **Local (n=47): local guideline or policy: 47 (100)%, DA chart: 47 (100%); SOP, 9 (19%); PIS, 14 (30%)**
Scotland	National and local	Scottish Palliative Care guidelines-Anticipatory Prescribing, 2019	• **National:** guideline only • **Local (n=13): local guideline or policy 12 (92%), DA chart, 13 (100%): SOP, 8 (62%), PIS, 7 (54%)**
Wales (1)	National-'Just in Case'	All Wales Just in Case Policy, 2018	• **National:** policy, PIS and 'All Wales' DA chart; supplemented by All Wales SC Guidance • **Local (n=5): no local documents** • Approach implemented to some degree in 3 out of the 5 HBs in addition to the 'targeted AP' approach
Wales (2)	National-'Targeted AP'	All Wales Care Decisions for the Last Days of Life Symptom Control Guidance, 2019	• **National:** guideline and 'Care Decisions' DA chart • **Local (n=5)**: **no local documents** • Sole approach in 2 out of the 5 HBs
Northern Ireland	National	RPMG Guidance for the Management of Symptoms in Adults in the Last Days of Life, 2018	• **National**: guideline and DA chart • **Local (n=3): no local documents** • National documents implemented in all settings

2) Document collection and inclusion for analysis



49 document sets included: 5 national and 44 local

Document analysis methods

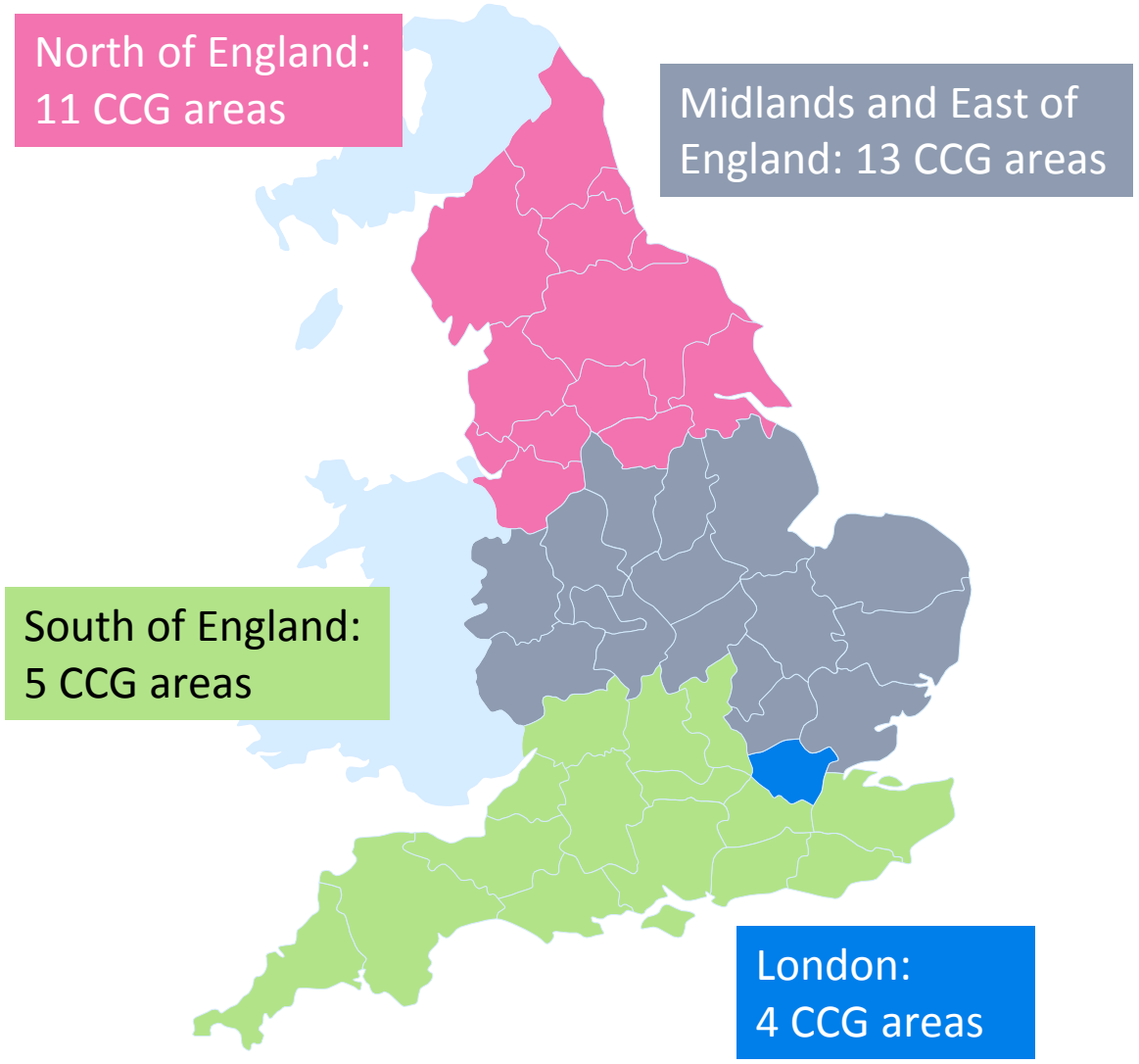
- Inclusion: professional facing documents (guidelines, policies, SOPs, DA charts, other)
- Exclusion: 1) patient information leaflets, 2) documents solely relating to inpatient or paediatric EOLC, 3) documents not referring to AP/JIC/pre-emptive prescribing

- Where multiple documents (‘document set’) per area, analysis focused on main document and accompanying DA chart

- Quantitative: domain frequency
- Qualitative: domain content

- 5-phases of AP used as an analytic framework
- Data extraction sheet (35 Qs) developed iteratively
- Data extraction sheets imported into NVivo 12

Local England sample (33 sets)



National documents (5 sets)

Country	Documents
England	NICE Care of Dying Adults in the Last Days of Life (NG31), 2015
Scotland	Scottish Palliative Care guidelines- Anticipatory Prescribing, 2019
Wales (1)- JIC	1) All Wales Just In Case Policy 2) All Wales DA chart
Wales (2)- AP	1) All Wales Care Decisions for the Last Days of Life Symptom Control Guidance, 2019 2) All Wales Care Decisions DA chart
Northern Ireland	1) Regional Palliative Medicine Group (RPMG) Management of Symptoms in Adults in the Last Days of Life, 2018 2) Regional DA chart

Document analysis results

1. Typology of approach to AP

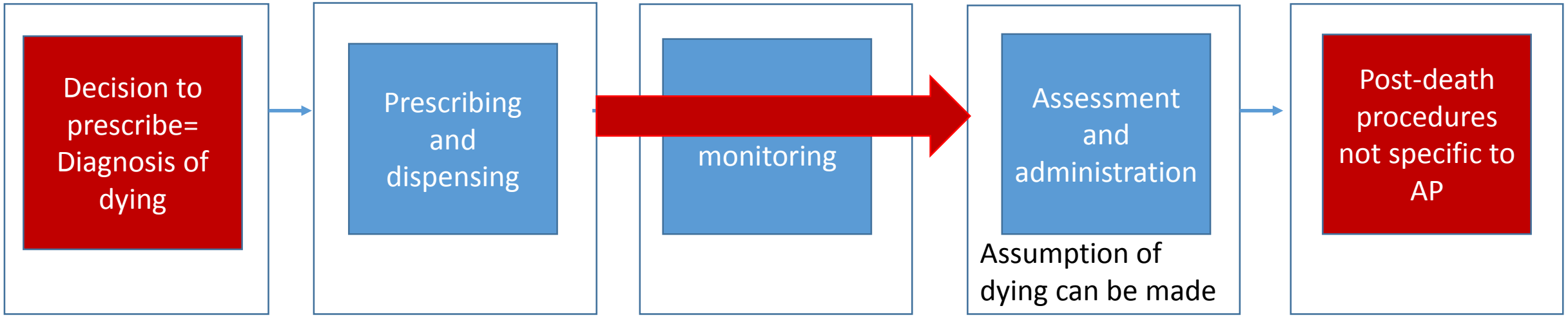
2. Gaps in AP guidance (domain frequency analysis)

3. Range of content in AP guidance (domain content analysis)

Typology of approach to AP

	Type 1 ('Last Days of Life Care') N= 24 (49%)	'Type 2 ('Anticipatory Care) N=16 (33%)	Other N=9 (18%)
Document number	**21 local documents**: England: 20 (60%) Scotland: 1 (9%) **3 national documents**: 1) England 2) Northern Ireland 3) Wales: targeted AP (All Wales Care Decisions)	**14 local documents**: England: 6 (18%) Scotland: 8 (73%) **2 national documents**: 1) Wales JIC policy 2) Scotland	9 local documents
Document type	Usually AP guidance is embedded within a 'Symptom Management in the Last Days of Life' guideline	AP guidance usually within a standalone AP-specific document which aims to guide the AP process	Mixture of the two

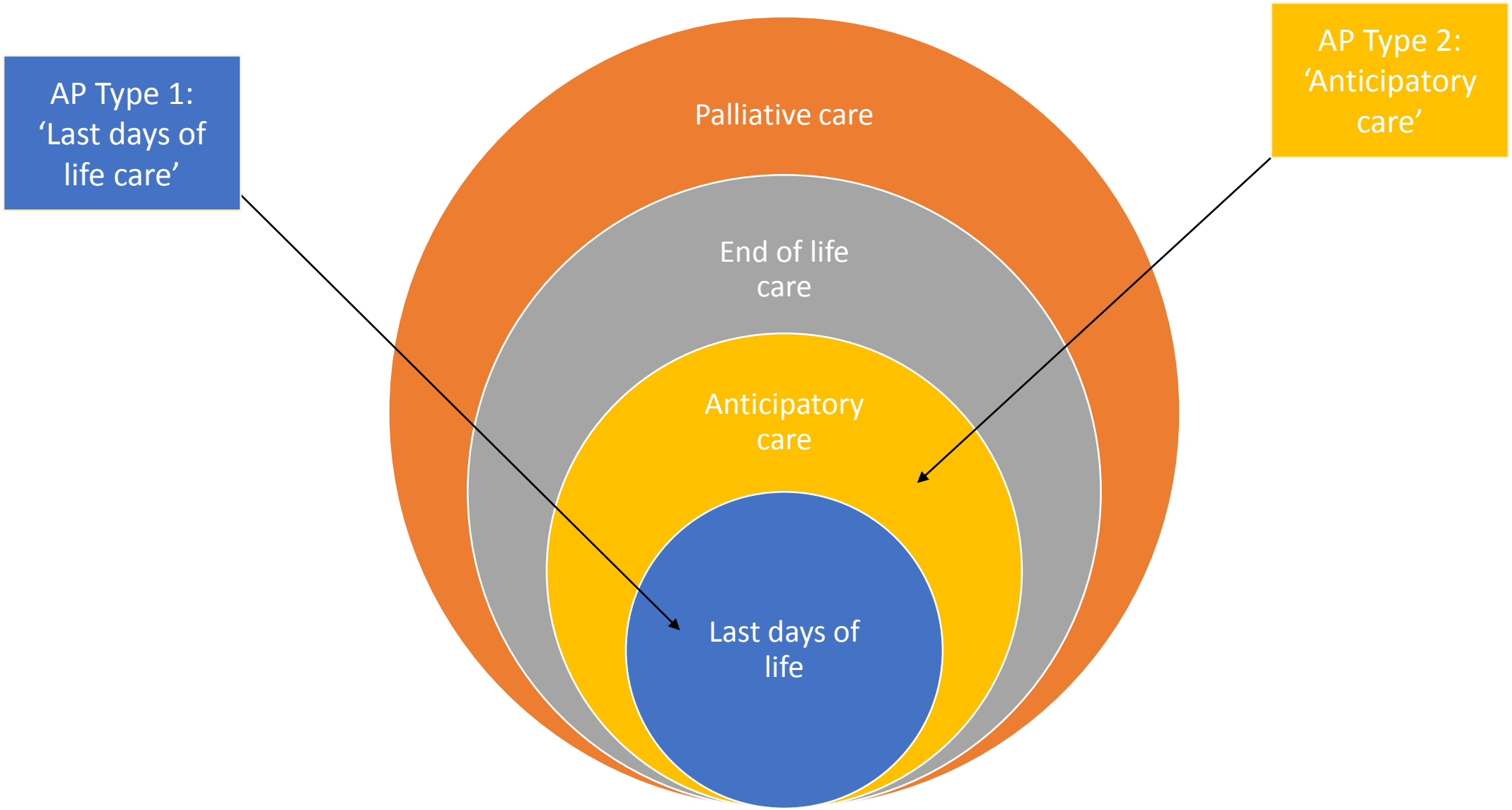
Type 1: ‘Last days of life care’



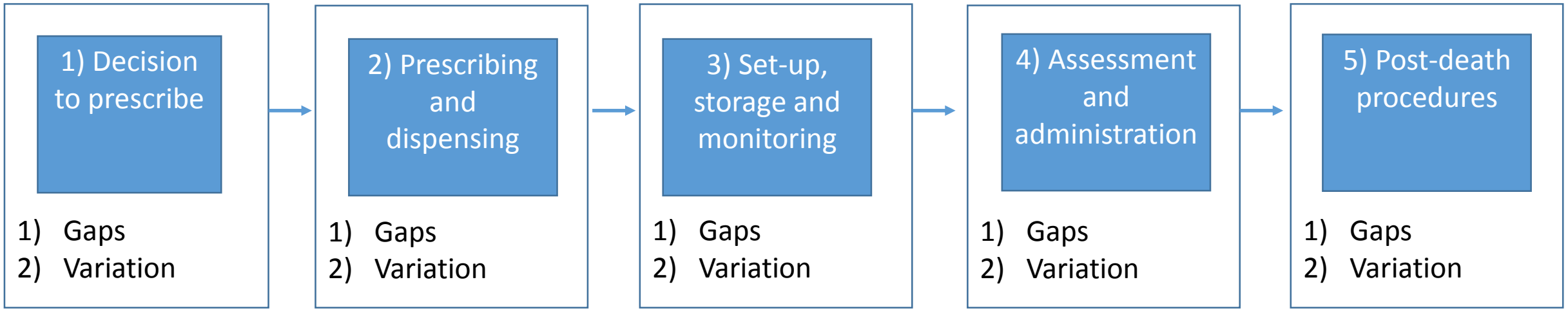
1. AP is a component of ‘last days of life care’ and is contained within this
2. No recognition that the ‘decision to prescribe’ may predate the dying phase
3. Limited acknowledgement of the time gap between prescribing and administration- no requirement for monitoring guidance
4. Procedures and processes related to ‘last days of life care’ rather than ‘AP’ per se

Type 2: ‘Anticipatory care’

1. AP is described as a process or a system operating within the wider system of palliative and end of life care
2. Decision to prescribe anticipatory meds separate from the diagnosis of dying
3. Time gap between prescribing and administration, with an asymptomatic ‘dormant’ phase
4. Specific risks of the system acknowledged with consent required
5. **Variation in how the transition from ‘prescribing’ to ‘administration’ is perceived and regulated**


AP Type 1: 'Last days of life care'
AP Type 2: 'Anticipatory care'
Palliative care
End of life care
Anticipatory care
Last days of life

Domain analysis



6) Overall system components: training & education, roles and responsibilities, process description

Domain 1: Decision to prescribe gaps

	All Wales Just in Case	All Wales targeted AP	Northern Ireland	National England	National Scotland	Local England Yes, N (%) N=33	Local Scotland Yes, N (%) N=11
Comprehensive inclusion criteria	✓	X	X	X	✓	11 (33)	6 (55)
Exclusion criteria	✓	X	X	X	X	6 (18)	7 (64)
Communication with patient or carer	✓	X	✓	✓	X	20 (61)	9 (82)
Communication between services	✓	X	X	✓	X	14 (42)	9 (82)

Domain 1: Decision to prescribe content

- Type 1: ‘When’ to prescribe is usually not explicitly addressed
- Type 2 approach: ‘When to prescribe’ usually addressed with inclusion and exclusion criteria

- ‘When’ to prescribe was described in a range of ways, with reference to:
  - Prognosis
  - Trajectory of deterioration (present or expected)
  - Prognostic tools
  - Disease stage
  - Swallowing difficulties
  - ‘Intuition’- *‘as early as possible’*
  - Other factors: ease of access to medications, care setting, patient/carer agreement, engagement in advance care planning

- Exclusion criteria- usually consistent across documents:
  - 1) Risk of drug diversion following risk assessment
  - 2) Patient (or carer) declines
  - Notable exception: one document (E19) had ‘current active treatment’ as an exclusion criterion in addition

- 2 parts to decision-making: 1) identification (DN/CNS/GP), 2) discussion (*‘the team caring for the patient’*)
- Communication around decision to prescribe described to a variable extent

'When' descriptor	N (documents)	Details
Prognosis	13 local 2 national	**>3 months (n=2):** *'the just in case box should be issued in anticipation of need, with the aim for it to be in place* ***several months*** *before it is likely to be needed'* (E14) **< 3 months (n=13)**: *'2-3 months'* (n=2), *'Weeks'* (n=3), *'Weeks or days'* (n=6) *'Approaching the last days'* (n=2)
Trajectory of deterioration	9 local documents 2 national documents	Current deterioration (n=3) Future trajectory (n=5) Combination (n=3) *'the patient's illness is deteriorating or anticipated to deteriorate suddenly……..'* (S9)
Prognostic tool	2 local documents	GSF amber (E1) Palliative Performance scale (PSS) ≤30% (S2)
Disease stage	16 local 2 national	'Terminal or life-limiting illness' (n=7) 'at the end of life' (n=4) 'Dying' (n=4) Need for palliative care support or on register (n =2)
Swallowing difficulties	4 local	Current or anticipated Usually described in conjunction with a 'prognosis' or 'trajectory' descriptor *'all patients who are in the last few days or weeks of life to treat new symptoms or when patients become unable to swallow' (E11)*
'As early as possible'	6 local 1 national	**Type 1:** *'as early as possible'* **Type 2:** *'act sooner rather than later!! The very fact you are considering AP indicates that it may be needed' (S9)*
Other	Advance care planning engagement (n=2), ability to access medications (location, time) (n=4), agreement from patient/carer (n= 4 inclusion criteria), discharge from hospital to community (n=3)	

Step 1: Communication guidance content

Type 2 ‘anticipatory care’ documents (AP-specific)	Type 1 ‘Last days of life care’ approach (Drug use)
1) What AP is: purpose, process, reassurance of what it is not	Medication details: risks, benefits, sedation (Not specific to AP)
2) Consent: permission to leave drugs in the home, option of ‘opting out’ must be discussed, as well as alternatives	
3) Need to provide written information	
4) Patient/carer responsibilities: who to call if symptoms, return of unused drugs to pharmacy	
5) Safety and legal issues e.g. ‘drugs are for professional use only’, storage requirements	
6) Contextual factors: current wishes, needs, meds, ACP	
7) Logistical aspects: how to collect drugs from pharmacy	

Domain 2: Prescribing and dispensing

Domains	All Wales just in case	All Wales targeted AP	Northern Ireland	National England	National Scotland	Local England N (%) N=33	Local Scotland N (%) N=11
Prescribing guidance on 4 main symptoms	✓ 1st line drugs	✓ All drug options	✓ 1st line drugs	✓ Drug class suggestions	✓ 1st line drugs	33 (100)	10 (91%)
Acute terminal events	X	X	X	✓	✓	17 (52)	2/10 (20)
Renal failure	✓	✓	✓	X	✓	28 (85)	9/10 (90)
Regular oral opioids	✓	✓	✓	X	✓	31 (94)	9/10 (90)
Opioid patches	✓	✓	✓	X	X	26 (79)	5/10 (50)
Advice on when to seek help	✓	✓	✓	✓	✓	32 (97)	10 (100)
Advice on where to seek help	✓	✓	✓	✓	✓	32 (97)	9 (82)

Where DA chart available:

Domains	All Wales just in case	All Wales targeted AP	Northern Ireland	Local England N (%)	Local Scotland N (%)
Pre-printed doses for PRN meds?	X	X	X	12/28 (43)	6/9 (67)
If dose ranges used for PRN meds, is there a statement to *'start at the lowest dose'* either DA chart or guideline?	✓	X	✓	Dose ranges used in 25/28 (89%) Statement present: 6/25 (24)*	Dose ranges used in 4/9 (44%) Statement present: 1/4 (25)
Is there explicit guidance around anticipatory syringe drivers?	X	X	X	13/29 (45)	0

*By contrast, often included with respect to syringe driver dose ranges

Domain 2: Prescribing and dispensing- content

- Both types of approaches to AP governance cover this is some detail: ‘type 1’ documents are particularly detailed and often used as appendices in ‘type 2’ documents. ‘Type 2’ documents focuses more on ‘process’ aspects (writing FP10, DA etc.)

- **Balance between standardised and individualised approaches:** differs between nations
- Most local guidelines suggest first line medication for the core 4-5 symptoms
- Individualised prescribing mainly pertains to ***‘special populations’***:
  - *Certain diagnoses: renal, liver and heart failure, Parkinson’s Disease, dementia, frailty, respiratory and neurological disease*
  - *Certain medication groups: regular opioid patches or oral opioids*
  - *Certain syndromes/complications: Bowel obstruction, terminal haemorrhage*
- ***Relationship between standardisation and individualisation***

- **Variation:** mainly relates to max doses and minimum dosing intervals
- Confusing and variable terminology used for ‘agitation’ states: *‘terminal agitation/restlessness’, ‘agitation at the end of life’, ‘mental anguish’, ‘distress’, ‘anxiety’, ‘non-specific agitation’, delirium’*

National guidance: variation across different nations of the UK

	All Wales targeted AP (Care Decisions)	All Wales JIC	Northern Ireland	National England	National Scotland
Pain or breathlessness (opioid naïve)	Morphine or diamorphine 2.5mg 2 hrly No max stated	Diamorphine 1st line Dosing as per 'Care Decisions'	Morphine 2 to 5mg 2-4 hrly No max stated	Not stated- 'individualised'	Morphine 2mg hrly Max of 6 doses/24 hrs. Seek advice if 3 doses in 4 hrs
Agitation	Midazolam (anxiety): 2.5mg **or** 5 mg 2 hrly Haloperidol (delirium): 2.5mg 4 hrly No max stated	Midazolam 1st line. Dosing as per 'Care Decisions'	Midazolam (anxiety, delirium and agitation): 2 to 5mg 2-4 hrly No max stated	Anxiolytic for anxiety or agitation Antipsychotic for delirium or agitation	Midazolam (anxiety or agitation): 2mg hrly Max of 6 doses/ 24 hrs. Seek advice if 3 doses in 4 hrs.
N&V	1st line: Cyclizine or Haloperidol 2nd or 3rd line: Levomepromazine	Cyclizine 1st line	Cyclizine 1st line	Not stated- 'individualised'	Levomepromazine 2.5 to 5mg **12 hrly**
Respiratory secretions	Hyoscine **H**ydrobromide OR Glycopyrronium	Hyoscine **H**ydrobromide	Glycopyrronium	**All 3 types** of drugs suggested	Hyoscine **b**utylbromide

Variation across local English documents

Pain in opioid naïve patients (n=33 documents)	
Starting dose (n=33)	**N (%)**
Morphine (n=19)	2.5-5mg: 15 (79%)
Diamorphine (n=9)	2.5-5mg: 8 (24)
Morphine or diamorphine (n=5)	2.5-5mg: 3 (9) Lower doses for diamorphine (2.5mg or 1.25-2.5mg)= 2 (40%)
Minimum interval between doses (n=33)	**N%**
1 hour or 1-2 hours	18 (55)
2 hours or 2-4 hours	11 (30)
30-60 min or 'do not repeat within 30 min'	3 (9)
Not stated	1 (3)
Maximum 24 hour dose (n=33)	**N (%)**
No maximum suggested	22 (67)
Max of 20mg- 30mg/24 hrs	5 (15)
Max of 60mg/24 hours	1 (3)
Syringe driver dose >100-200mg/24hrs	2 (6)
Call for help if after 2-3 doses	3 (9)

Variation across local English documents

Agitation	
Starting dose for Midazolam (n=33)	**N (%)**
2.5-5mg OR 2-5mg	26 (79)
2.5mg	6 (18)
2.5-10mg	1 (3)
Minimum interval between doses (n=33)	**N%**
1 hour	11 (33)
2 hours	9 (27)
2-4 hours OR 4 hours	6 (18)
30-60 min or ‘do not repeat within 30 min’	5 (15)
Not stated	2 (6)
Number of doses in a 24 hour period or maximum 24 hour dose (n=33)	**N (%)**
No maximum suggested	8 (24%)
10-20mg/24hrs	3 (9)
30mg/24hrs	11 (33)
60-80mg/24hrs	7 (21)
Call for help if 2 doses needed 1 hour apart or 3 over 4 hours or 3 over 24 hrs	4 (12)

Relationship between standardisation and individualisation

	National Scotland	National Wales
Standardisation	1) 1st line drug for 4 main symptoms specified 2) Dosing suitable for 'high-risk' frail elderly opioid-naïve patient • Examples: • Agitation: Midazolam 2.5mg hourly, Levomepromazine only under specialist advice	1) Drug options listed with doing information for each e.g. Haloperidol or Cyclizine 2) Dosing suitable for 'average' opioid-naïve patient • Examples: • Agitation: Midazolam 2.5 or 5mg, Haloperidol 2.5mg
Individualisation	For renal failure	For: 1) Renal failure 2) Heart failure 3) Parkinson's disease 4) (Not stated in document, but may need to reduce down doses in elderly)

1) Standardisation provides a framework or anchor against which individualization can occur

2) The more populations you can accommodate within standardization, then less individualization needed

Domain 3: Set-up, storage monitoring

	All Wales- just in case	All Wales- targeted AP	Northern Ireland	National England	National Scotland	Local England N=33 N (%)	Local Scotland N=11 N (%)
Monitoring during the asymptomatic phase	✓	X	✓ (vague)	✓ (vague)	X	15 (45)	6 (54)
Storage	✓	X	X	X	X	7 (21)	8 (72)
Equipment	✓	X	X	X	✓	8 (24)	9 (82)
Stock monitoring process	✓	X	X	X	X	14 (42)	7 (64)

Domain 3: Storage and monitoring

- Rarely covered in the ‘type 1’ ’last days of life care’ approach but more common in the ‘type 2’ approach

- Frequency of monitoring during asymptomatic phase variable:
  - Often not specified: ‘*be regularly reviewed’ (E1)*
  - *‘At least every 4 weeks’* (E11, E14)
  - *‘Every 2 weeks’* (E2, E19)
  - *‘Weekly’* (S8)
  - After any known change in circumstance

1) Supply monitoring:

‘Checks must be made at least once every 4 weeks ***to ensure that nothing has been removed, used or expired*** *without a record being made’ (E11)*

2) Prescription monitoring:

‘An identified doctor or nurse must be responsible for ensuring that regular review of required drugs takes place, (at least once a month, and/or after any known change in circumstances). This will help ***to ensure that drugs in the ‘Just in Case’ are appropriate and relevant*** *both in terms of strength and type’ (E14)*

Domain 4: Assessment and administration

Domains	All Wales- just in case	All Wales- targeted AP	Northern Ireland	National Scotland	National England	Local England N=33 (%)	Local Scotland N=11 (%)
Guidance on assessment prior to administration	✓	✓	✓	✓	✓	25 (76%)	5 (45)
Advice on reversing treatable factors	✓	✓	✓	✓	✓	23 (70%)	4 (36)
Monitoring or reassessment after treatment	✓	✓	✓	✓	✓	26 (79%)	10 (91)

Domain 4: Assessment and administration

- Type 1:
- Detailed symptom assessment guidance, but administration phase is rarely distinguished from prescribing phase and, therefore, no sense of a ‘transition period’ between the two
- Particular risks of administering pre-emptive medications not addressed

- Type 2:
- Symptom assessment often not addressed in the main document but supplementary ‘last days of life symptom management guidance’ usually referred to.
- Though there is acknowledgement of the distinction between prescribing and administration phases, the conditions for administering the first injection are rarely made explicit

- Most pre-administration assessment guidance relates to terminal agitation including its distinction from delirium

- Different approaches to transitioning from the asymptomatic period to the symptomatic are taken within type 2 documents.

‘Transition from asymptomatic to symptomatic phase’- different strategies

1) Asymptomatic phase monitoring

- Weekly/2 weekly/4 weekly review review of Px

2) Safety netting before first administration

- Highlighting need for assessment and potential wrong assumptions
- Highlighting conditions for medical review
- Option for prescriber to highlight on drug chart if they wish for the nurse to contact a doctor before administration
- 2-stage approach to prescribing: FP10 first, DA chart later when nearer time of death

3) Safety-netting after administration

- Requirement to inform GP surgery if meds used
- Requirement to phone for medical advice after first administration to establish onward plan
- Thresholds and timeframes for medical review/specialist advice

'It should not be assumed that the presence of a Just in Case box means that no active intervention is appropriate. Each patient will need to be assessed individually, and action taken as required’ (E14)

Domain 5: Post-death procedures

	All Wales-just in case	All Wales-targeted AP	Northern Ireland	National Scotland	National England	Local England N=33 N (%)	Local Scotland N=33 N (%)
Advice on return to pharmacy and disposal	✓	X	X	X	X	8 (24)	9 (82)
Evidence of an audit process or plan	✓	X	X	X	X	5 (21)	5 (15)

'A healthcare professional should tell the patient's relative/carer to return the unused drugs to a community pharmacy for destruction. This should be documented in the patient's community nursing record. If a JiC box was in use it should be returned to the District Nurse, cleaned in line with the Infection Control Policy, re-labelled and kept ready for re-use' (E19)

Domain 6: Description of the overall system

	All Wales- just in case	All Wales- targeted AP	Northern Ireland	England national	Scotland national	England local	Scotland local
Overall process description	✓	X	X	X	✓	7 (21)	9 (82)
Comprehensive description of **roles and responsibilities** defined	✓	X	X	X	X (limited only')	5 (15)	8 (73)
Comprehensive description of **training and competencies**	✓	X	X	X	X	5 (15)	0

Summary

- 2 different approaches relating to location within EOLC
- Gaps in England: 1) decision to prescribe, 2)set-up, storage, monitoring, 3) drug disposal, 4) transition from administration to prescription, 5) overall system description (roles & responsibilities, training etc.)
- Variation in England: mainly relates to the prescribing phase

Recommendations for principles for guidance development

1. Be clear about where AP is located within EOLC
   - Last days of life?
   - Last year of life?

2. Think about what things are specific to AP (as opposed to EOLC)
   - How does prescribing in advance differ from reactive prescribing?
   - How does administering an anticipatory medication differ from one that has been reactively prescribed?

3. Think the complementary relationship between standardisation and individualisation

4. Think about the mechanism and purpose of AP
   - Is it about access to medications?
   - Is it about reducing OOH works?

Acknowledgements

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