# SUPPLEMENTARY MATERIAL

**Appendix 1:** Description of potential barriers and strategies prompted by the eCRD (electronic data collection form) to guide pharmacists during the provision of the intervention.

a. Potential barriers and their associated strategies targeted at non-adherent patients. These were tailored according to the patient's individual needs.

| Practical barrier (Non-intentional non-adherence) | Recommended strategy to increase capacity |
|---|---|
| **Lack of patient knowledge (about the prescribed medications, instructions or consequences of non-adherence)** | Provide verbal and written information about the condition and the medications prescribed to treat it (e.g. what they are for and how to take them) <br><br> Provide inhaler/spacer technique training (only for patients diagnosed with asthma or COPD) |
| **Presence of cognitive barriers (e.g. confusion, lack of attention)** | Prepare a medicines list |
| | Provide a Dose Administration Aid (DAA) |
| **Presence of physical barriers (e.g. swallowing difficulties, trembling, difficulties with inhaler use)** | Contact the patient's GP to suggest a simplification or modification of the medication regimen or |
| | Suggest or contact the patient's GP to recommend a DAA |
| **Complexity of treatment (e.g. dosing regimen, polypharmacy)** | Prepare a medicines list |
| | Provide a DAA |
| | Contact the patient's GP to suggest a simplification of the medication regimen |
| **Forgetfulness (e.g. difficulty to remember to take a medication, routine changes)** | Set up a medication reminder system (e.g. SMS reminders and alarms) |
| | Link medication taking to daily activity |
| | Set up a medication management app |
| **Lack of family support** | Provide self-management strategies (e.g. self-monitoring) <br><br> Involve a family member on the medication management process |
| Perceptual barrier (Intentional non-adherence) | Recommended strategy to address the perceptual barrier |
| **Wrong beliefs regarding the condition** | Address wrong beliefs by educating the patient on the condition and the medications prescribed to treat it |

| | |
|---|---|
| **Wrong beliefs regarding the medications prescribed:**<br><br>• **Low perceived necessity for taking the medication**<br>• **High concerns about taking the medication** | Increase the perceived severity and susceptibility to disease by:<br><br>• Explaining the severity of the disease and the reasons behind taking the medication on a regular basis<br>• Explain the potential risks of not taking the medications as prescribed. Explain how the medication can help to control the condition and it associated symptoms and how it can prevent future worsening events<br><br>Increase perceived benefits of medication adherence<br>Decrease potential concerns regarding the use of the medication.<br>Explain the probability of suffering potential side effects and address how to manage them if they appear |
| **Perception/Social stigma (Shame of taking the medication in public, in the work place, in front of family relatives and friends)** | Reinforce the need of taking the medication at the right time<br>Modify potential beliefs about social stigma related to the use of the medication |
| **Absence of symptoms (e.g. asymptomatic nature of the disease, clinical improvement)** | Educate on the condition, emphasizing the need of taking the medication even in the absence of symptoms<br><br>Highlight the importance of taking the medication in order to achieve the target clinical outcomes |
| **Lack of motivation (e.g. Depression, lack of perception of clinical improvement)** | Reinforcement of knowledge regarding the condition, enquiring for factors that cause a lack of motivation<br><br>Highlight the importance of taking the medication and associate it with future improvements on clinical outcomes and quality of life<br><br>Provide positive reinforcement on actions undertaken by the patient<br><br>Goal-setting and clinical outcomes monitoring |
| **Patient-health care provider communication (e.g. lack of patient confidence on the health care provider, inaccurate communication)** | Provide positive reinforcement of the prescriber's criteria<br><br>Improve the trust between the health care provider-patient |

b. Strategies targeted at adherent patients. These were tailored according to the patient's individual needs.

| Recommended strategy | Description |
|---|---|
| **Educate regarding the medication** | Provision of education on the medication prescribed, assessing any queries regarding medication and disease management. Provision of verbal and written information when needed |
| **Educate regarding the condition** | Provision of education on the condition, providing verbal and written information when needed |
| **Educate regarding the importance of medication adherence** | Educate on the concept of medication adherence and its impact on health outcomes and quality of life. Provision of positive reinforcement of adherence behavior |
| **Motivate/Recognise accomplishments** | Pharmacist-patient review of clinical outcomes and adherence, recognition of achievements; goal setting and motivation to persist adherent. |
| **Educate on clinical outcomes targets** | Education on clinical outcomes targets |
| **Solve other questions** | Treatment changes, lifestyle changes |

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance
placed on this supplemental material which has been supplied by the author(s)

*BMJ Qual Saf*

**Appendix 2:** Number of participants each outcome was collected from and rate (%) of missingness in follow-up visits by treatment group

| Outcome | Number of eligible participants | Visit number | Control | Intervention |
|---|---|---|---|---|
| Adherence | n: Control=553, Intervention=633 | 1 | 0% | 0% |
| | | 2 | 14% | 9% |
| | | 3 | 11% | 12% |
| | | 4 | 13% | 15% |
| | | 5 | 17% | 17% |
| | | 6 | 13% | 12% |
| Systolic Blood Pressure (mmHG) | n: Control=217, Intervention=283 | 1 | 0% | 1% |
| | | 2 | 15% | 7% |
| | | 3 | 11% | 11% |
| | | 4 | 10% | 11% |
| | | 5 | 14% | 13% |
| | | 6 | 9% | 8% |
| Diastolic Blood Pressure (mmHG) | n: Control=217, Intervention=283 | 1 | 0% | 1% |
| | | 2 | 15% | 7% |
| | | 3 | 11% | 11% |
| | | 4 | 10% | 11% |
| | | 5 | 14% | 13% |
| | | 6 | 9% | 8% |
| Hypertension diagnosis | n: Control=217, Intervention=283 | 1 | 0% | 1% |
| | | 2 | 15% | 7% |
| | | 3 | 11% | 11% |
| | | 4 | 10% | 11% |
| | | 5 | 14% | 13% |
| | | 6 | 9% | 8% |

| Outcome | Number of eligible participants | Visit number | Control | Intervention |
|---|---|---|---|---|
| CCQ score | n: Control=154, Intervention=145 | 1 | 0% | 0% |
| | | 2 | 14% | 11% |
| | | 3 | 12% | 11% |
| | | 4 | 16% | 14% |
| | | 5 | 23% | 20% |
| | | 6 | 19% | 14% |
| CCQ binary (low clinical impact) | n: Control=154, Intervention=145 | 1 | 0% | 0% |
| | | 2 | 14% | 11% |
| | | 3 | 12% | 11% |
| | | 4 | 16% | 14% |
| | | 5 | 23% | 20% |
| | | 6 | 19% | 14% |
| ACQ score | n: Control=180, Intervention=205 | 1 | 1% | 0% |
| | | 2 | 12% | 10% |
| | | 3 | 10% | 15% |
| | | 4 | 13% | 20% |
| | | 5 | 15% | 20% |
| | | 6 | 11% | 16% |
| ACQ binary (asthma control) | n: Control=180, Intervention=205 | 1 | 1% | 0% |
| | | 2 | 12% | 10% |
| | | 3 | 10% | 15% |
| | | 4 | 13% | 20% |
| | | 5 | 15% | 20% |
| | | 6 | 11% | 16% |

**Observation:** Linear and generalised linear mixed models for the study outcomes were used, allowing for the assumption of 'missing-at-random' (i.e. missing contingent on values included in the regression model) without requiring imputation for the missing outcomes.

**Appendix 3:** Study outcomes

| 1. CATEGORICAL VARIABLES | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Comparison** | **Percentage of Patients (95%CI)** | | **Odds Ratio (95% CI)** | **p-value** | **Percentage of Patients (95%CI)** | | **Odds Ratio (95% CI)** | **p-value** |
| | **CG** | **IG** | | | **CG** | **IG** | | |
| a) Medication Adherence: Adherent patients n: Control=553, Intervention=633 | | | | | b) Hypertension control n: Control=219, Intervention=283 | | | |
| At visit 1 | 44.3% (37.0-51.8) | 39.1% (32.6-46.0) | 0.82 (0.54 - 1.24) | 0.34 | 52.9% (45.2%-60.5%) | 55.5% (48.5%-62.3%) | 1.11 (0.73 - 1.68) | 0.63 |
| At visit 2 | 61.9% (54.3-68.9) | 68.7% (62.2-74.6) | 1.39 (0.91 - 2.13) | 0.13 | 55.4% (47.3%-63.2%) | 58.2% (51.1%-65.0%) | 1.12 (0.73 - 1.73) | 0.61 |
| At visit 3 | 66.2% (58.9-72.8) | 79.8% (74.4-84.3) | 2.06 (1.33 - 3.19) | 0.0012* | 57.9% (49.9%-65.5%) | 62.2% (55.0%-68.8%) | 1.20 (0.77 - 1.85) | 0.42 |
| At visit 4 | 65.1% (57.7-71.9) | 86.9% (82.7-90.2) | 3.60 (2.28 - 5.67) | <0.0001* | 59.5% (51.5%-67.0%) | 65.3% (58.2%-71.7%) | 1.28 (0.82 - 1.99) | 0.27 |
| At visit 5 | 67.0% (59.7-73.6) | 88.7% (84.8-91.7) | 3.97 (2.49 - 6.33) | <0.0001* | 57.1% (49.0%-64.8%) | 65.7% (58.6%-72.1%) | 1.44 (0.92 - 2.24) | 0.11 |
| At visit 6 | 66.5% (59.2-73.1) | 90.9% (87.5-93.4) | 5.12 (3.20 - 8.20) | <0.0001* | 63.8% (56.0%-71.0%) | 68.3% (61.5%-74.5%) | 1.22 (0.78 - 1.91) | 0.38 |
| **Overall** | | | **1.86 (1.24 - 2.81)** | **0.0030\*a** | | | **1.21 (0.87 - 1.70)** | **0.26a** |
| c) Asthma control n: Control=180, Intervention=205 | | | | | d) COPD low clinical impact n: Control=154, Intervention=145 | | | |
| At visit 1 | 43.8% (34.3%-53.8%) | 37.3% (29.0%-46.4%) | 0.76 (0.44 - 1.32) | 0.33 | 16.3% (10.7%-24.1%) | 20.6% (14.1%-29.1%) | 1.33 (0.68 - 2.60) | 0.40 |
| At visit 2 | 49.0% (38.9%-59.2%) | 49.4% (40.0%-58.8%) | 1.01 (0.58 - 1.77) | 0.96 | 22.5% (15.4%-31.8%) | 27.7% (19.6%-37.5%) | 1.31 (0.69 - 2.52) | 0.41 |
| At visit 3 | 51.8% (41.6%-61.8%) | 57.7% (48.0%-66.8%) | 1.27 (0.72 - 2.23) | 0.41 | 21.2% (14.3%-30.2%) | 40.8% (31.0%-51.4%) | 2.57 (1.35 - 4.87) | 0.0039* |
| At visit 4 | 48.6% (38.5%-58.9%) | 60.1% (50.3%-69.2%) | 1.59 (0.90 - 2.83) | 0.11 | 22.4% (15.2%-31.6%) | 40.0% (30.1%-50.7%) | 2.31 (1.22 - 4.40) | 0.0106* |
| At visit 5 | 48.9% (38.7%-59.2%) | 63.9% (54.2%-72.6%) | 1.85 (1.04 - 3.31) | 0.0369* | 27.0% (18.8%-37.1%) | 39.9% (29.9%-50.8%) | 1.80 (0.95 - 3.42) | 0.07 |
| At visit 6 | 57.8% (47.5%-67.5%) | 72.0% (63.1%-79.5%) | 1.88 (1.05 - 3.36) | 0.0339* | 29.2% (20.8%-39.4%) | 45.3% (35.0%-56.0%) | 2.01 (1.07 - 3.75) | 0.0294* |
| **Overall** | | | **1.28 (0.81 - 2.03)** | **0.29a** | | | **1.92 (1.13 - 3.25)** | **0.0151\*a** |

**2. CONTINUOUS VARIABLES**

| Comparison | Mean (95%CI) Systolic Blood pressure (mmHg) | | Mean difference (95% CI) between IG and CG | p-value | Mean (95%CI) Diastolic Blood pressure (mmHg) | | Mean difference (95% CI between IG and CG | p-value |
|---|---|---|---|---|---|---|---|---|
| | CG | IG | | | CG | IG | | |
| a) SBP<br>n: Control=219, Intervention=283 | | | | | b) DBP<br>n: Control=219, Intervention=283 | | | |
| At visit 1 | 136.6 (134.2-139.1) | 137.0 (137.8-139.2) | 0.37 (-2.96 - 3.70) | 0.83 | 79.1 (77.3-80.9) | 79.2 (77.6-80.8) | 0.08 (-2.34 - 2.49) | 0.95 |
| At visit 2 | 137.3 (134.8-139.8) | 136.1 (133.8-138.4) | -1.19 (-4.59 - 2.21) | 0.49 | 79.3 (77.5-81.1) | 78.1 (76.4-79.7) | -1.26 (-3.71 - 1.19) | 0.31 |
| At visit 3 | 136.1 (133.6-138.7) | 135.7 (133.4- 137.9) | -0.45 (-3.86 - 2.95) | 0.79 | 79.8 (77.9-81.6) | 78.1 (76.4-79.7) | -1.68 (-4.14 - 0.77) | 0.18 |
| At visit 4 | 136.9 (134.4-139.4) | 135.0 (132.7- 137.3) | -1.93 (-5.34 - 1.48) | 0.27 | 79.2 (77.4-81.0) | 77.5 (75.8-79.1) | -1.77 (-4.22 - 0.69) | 0.16 |
| At visit 5 | 136.6 (134.0-139.1) | 134.4 (132.1-136.7) | -2.20 (-5.63 - 1.23) | 0.21 | 80.0 (78.1-81.8) | 76.9 (75.2-78.5) | -3.08 (-5.55 - -0.61) | 0.0144* |
| At visit 6 | 134.8 (132.2-137.3) | 133.7 (131.4-135.9) | -1.10 (-4.49 - 2.29) | 0.53 | 79.6 (77.8-81.4) | 76.7 (75.1-78.3) | -2.88 (-5.33 - -0.43) | 0.0213* |
| **Overall** | | | **-1.06 (-3.99 - 1.88)** | **0.48[a]** | | | **-1.70 (-3.88 - 0.48)** | **0.13[a]** |

| Comparison | Mean score (95%CI) | | Mean Difference (95% CI) between IG and CG | p-value | Mean score (95%CI) | | Mean Difference (95% CI) between IG and CG | p-value |
|---|---|---|---|---|---|---|---|---|
| | CG | IG | | | CG | IG | | |
| c) ACQ score (0-6, 0= better clinical control)<br>n: Control=180, Intervention=205 | | | | | d) CCQ score (0-6, 0=better health status, low clinical impact)<br>n: Control=154, Intervention=145 | | | |
| At visit 1 | 1.17 (0.97-1.37) | 1.16 (0.98-1.35) | 0.00 (-0.27 - 0.27) | 0.98 | 2.10 (1.88-2.32) | 1.79 (1.57-2.01) | -0.32 (-0.63 - 0.00) | 0.0476* |
| At visit 2 | 1.12 (0.92-1.33) | 0.98 (0.79-1.17) | -0.14 (-0.42 - 0.13) | 0.31 | 1.92 (1.70-2.15) | 1.63 (1.40-1.85) | -0.30 (-0.61 - 0.02) | 0.07 |
| At visit 3 | 1.05 (0.84-1.25) | 0.90 (0.71-1.09) | -0.14 (-0.42 - 0.13) | 0.31 | 1.93 (1.71-2.16) | 1.45 (1.22-1.67) | -0.49 (-0.80 - -0.17) | 0.0026* |
| At visit 4 | 1.08 (0.87-1.28) | 0.80 (0.61-0.99) | -0.28 (-0.56 - 0.00) | 0.05 | 1.91 (1.68-2.13) | 1.38 (1.15-1.60) | -0.53 (-0.85 - -0.21) | 0.0011* |
| At visit 5 | 1.11 (0.90-1.31) | 0.71 (0.52-0.90) | -0.40 (-0.68 - -0.12) | 0.0056* | 1.82 (1.59-2.05) | 1.31 (1.08-1.54) | -0.51 (-0.83 - -0.18) | 0.0021* |
| At visit 6 | 0.91 (0.71-1.11) | 0.63 (0.44-0.82) | -0.28 (-0.56 - 0.00) | 0.0489* | 1.71 (1.49-1.94) | 1.21 (0.99-1.44) | -0.50 (-0.82 - -0.18) | 0.0022* |
| **Overall** | | | **-0.19 (-0.43 - 0.04)** | **0.11[a]** | | | **-0.43 (-0.73 - -0.14)** | **0.0035*[a]** |

[a] *LR P-value: Likelihood ratio p-value for the overall effect of the outcome.*
*\*Statistically significant*
*ACQ: Asthma Control Questionnaire, CCQ: Clinical COPD Questionnaire, CG: Control Group, CI: Confidence Interval, DBP: Diastolic Blood Pressure, IG: Intervention Group, SD: Standard Deviation*

**Appendix 4:** Percentage of adherent patients per clinical condition

| Comparison | Percentage of adherent Patients (95%CI) | | Odds Ratio (95% CI) | p-value |
|---|---|---|---|---|
| | Control Group (CG) | Intervention Group (IG) | | |
| **COPD** | | | | |
| At visit 1 | 47.6% (37.6%-57.9%) | 40.6% (31.1%-50.8%) | 0.75 (0.42 - 1.35) | 0.34 |
| At visit 2 | 62.3% (51.6%-71.9%) | 71.6% (61.7%-79.8%) | 1.53 (0.82 - 2.85) | 0.18 |
| At visit 3 | 66.6% (56.2%-75.6%) | 80.5% (71.8%-87.0%) | 2.07 (1.07 - 4.00) | 0.0297* |
| At visit 4 | 65.3% (54.7%-74.6%) | 87.9% (80.7%-92.7%) | 3.88 (1.90 - 7.90) | 0.0002* |
| At visit 5 | 66.4% (55.6%-75.8%) | 91.4% (84.9%-95.2%) | 5.36 (2.46 - 11.7) | <0.0001* |
| At visit 6 | 72.5% (62.3%-80.7%) | 92.9% (87.0%-96.2%) | 4.93 (2.20 - 11.1) | 0.0001* |
| **Overall** | | | **1.71 (1.01 - 2.91)** | **0.0465[a]*** |
| **ASTHMA** | | | | |
| At visit 1 | 31.5% (23.5%-40.8%) | 26.8% (20.0%-34.9%) | 0.79 (0.46 - 1.38) | 0.42 |
| At visit 2 | 60.1% (50.1%-69.3%) | 54.3% (45.1%-63.2%) | 0.79 (0.46 - 1.37) | 0.42 |
| At visit 3 | 56.7% (46.7%-66.2%) | 69.2% (60.2%-76.8%) | 1.71 (0.98 - 3.00) | 0.40 |
| At visit 4 | 54.1% (44.0%-63.8%) | 81.7% (74.2%-87.5%) | 3.80 (2.09 - 6.93) | 0.06 |
| At visit 5 | 57.2% (47.0%-66.8%) | 83.7% (76.5%-89.0%) | 3.85 (2.09 - 7.09) | <0.0001* |
| At visit 6 | 55.2% (45.1%-64.8%) | 85.% (78.2%-89.9%) | 4.59 (2.50 - 8.41) | <0.0001* |
| **Overall** | | | **1.86 (1.17 - 2.96)** | **0.0085[a]*** |
| **HYPERTENSION** | | | | |
| At visit 1 | 54.5% (44.0%-64.6%) | 45.7% (36.4%-55.2%) | 0.70 (0.40 - 1.24) | 0.22 |
| At visit 2 | 65.1% (54.5%-74.4%) | 77.8% (69.9%-84.2%) | 1.88 (1.02 - 3.46) | 0.0416* |
| At visit 3 | 75.8% (66.4%-83.2%) | 87.3% (81.3%-91.6%) | 2.20 (1.15 - 4.20) | 0.0171* |
| At visit 4 | 76.1% (66.8%-83.4%) | 91.1% (86.3%-94.4%) | 3.24 (1.65 - 6.34) | 0.0006* |
| At visit 5 | 77.7% (68.5%-84.8%) | 92.1% (87.5%-95.1%) | 3.34 (1.67 - 6.67) | 0.0006* |
| At visit 6 | 74.4% (64.9%-82.1%) | 94.8% (91.3%-96.9%) | 6.24 (3.05 - 12.7) | <0.0001* |
| **Overall** | | | **1.67 (0.98 - 2.85)** | **0.06[a]** |

[a] LR P-value: Likelihood ratio p-value for the overall effect of the outcome.

*Statistically significant

**RESULTS:** The trends in the three conditions were similar, with an increase on the percentage of adherent patients at the end of the study. Statistically significant differences between intervention and control groups were observed earlier in COPD (starting at visit 3) and hypertension (starting at visit 2).