Piloting the development of an evidence-based care pathway: pharmacological treatment of adults with essential hypertension in a primary care setting in Jordan

Final Report for the World Bank and the Department of Health (UK)

Background

In March 2009, the World Bank sponsored a workshop organised in the Dead Sea to offer training on the basic principles and methods for health technology assessment (HTA) and best clinical practice standards, discuss the governance framework for applying these to policy making and set out a realistic plan of action for implementing such guidelines in Jordan. During that same workshop, hypertension and diabetes were identified as high burden of disease areas and hence priorities for policy development. The workshop participants, representing all major stakeholders in health policy in Jordan, agreed that a pilot in developing an evidence-based guideline in one of the priority areas would be a valuable exercise for Jordanian policy makers and practitioners.

Clinical guidelines, when developed in a transparent and inclusive process and adapted to the local system, can help:

- Spread good practice and reduce inappropriate variation, especially in public sector primary care settings
- Ensure efficient investment of limited resources and improved outcomes through rational drug use
- Form the basis of a national initiative to raise awareness of the disease and the best way to treat it, amongst patients, doctors, other healthcare professionals and the general public
- Improve drug availability through better needs forecasting and more targeted procurement, which allows more effective (in terms of types and volume) ordering of drugs to meet the population's needs

In June 2009, NICE, with the support of the World Bank, ran a three-day guideline development workshop/training session in Amman. This was the first phase of a two-part pilot, and its aim was to initiate the development of an evidence-based treatment care pathway for one of the high priority disease areas identified in the Dead Sea meeting, hypertension. A number of senior clinicians, including specialists and general practitioners, policy makers and health economists, participated in the training and the discussion as Guideline Development Group (GDG) members (see Appendix A). These discussions informed further analytical work undertaken by a core technical team with UK and Jordanian expertise in clinical medicine, pharmacy?, health economics

and systematic reviewing (see Appendix B). This work subsequently informed the second phase of the pilot, in which the final output, an evidence based treatment algorithm adapted to the Jordanian setting, was developed.

This paper describes the process and methods used for the pilot, the final outputs and the challenges and opportunities for further work in strengthening evidence-informed policy making structures and building the necessary support capacity in middle income countries, such as Jordan.

This pilot was sponsored by the World Bank and the UK's Department of Health. MeTA Jordan, a DFID-sponsored initiative, offered its full support throughout the pilot.

Phase I of the pilot

Below we describe the activities that took place in preparation for and during Phase I of the pilot (before and during our first visit to Amman). Phase I of the pilot consisted of: (a) a pre-visit stage, where relevant NICE material was collected and analysed, the technical and GDG teams were convened and the programme of training and work for both visits was developed; and (b) a three-day visit to Amman. Day 1 was devoted to working with the Jordanian technical team and Days 2 and 3 formed the first GDG meeting, which included training, clinical question development and identification of Jordanian evidence and data sources to inform guideline adaptation to the Jordanian system.

a. *Compilation of relevant material and preliminary analysis including:* the evidence base including systematic reviews and economic analysis for the NICE guideline on the pharmacological treatment of hypertension; major clinical studies published since the NICE guideline; other major international guidelines (USA (JNC VII) and European (ESH/ESC)); and Jordanian/Middle Eastern clinical and epidemiological data including prevalence, variation in practice and costs.

b. *Convening the guideline development group and the technical and administrative teams*: Three groups of Jordanian experts were convened: the guideline development group (GDG) – and a GDG Chair; the systematic reviewers and health economists supporting the group and a project manager coordinating the activities. The activity of identifying and convening the experts was led by MeTA Jordan.

c. *Hands-on training*: Training on clinical guideline development was carried out for the GDG (Day 2) and technical experts (Day 1) along the lines of the training NICE provides to its own groups, with the addition or expansion of elements of particular relevance to the Jordanian setting. The training was interactive and served as the first stage in the guideline development process. It focused on scoping and identifying key clinical questions; chairing/working with multi-stakeholder groups; managing

conflict of interest and operating contestability mechanisms; incorporating social values and expert opinion; organising and responding to public consultation; engaging with patient groups and developing lay-friendly versions of the guideline and, finally, methods for supporting the implementation of the recommendations in a guideline and assessing its overall budget impact. An overview of the methods for systematic reviewing and critical appraisal and of economic evaluation of healthcare interventions was also provided to help the discussions on Day 3.

d. *Guideline development (1st GDG)*[1]:

- Framing discussions: Discussions in Days 2 and 3 focused on current practice and need for hypertension management in Jordan, the split between different health providers, standards of care and compliance with international (mostly US) treatment guidelines and cost implications of management practices. It became apparent that hypertension management in the secondary care setting is of a high standard across the major academic, private and military institutions in the country. However, the patient population in secondary and tertiary care is not representative of those presenting in a primary care setting (although, due to delayed presentation/diagnosis co-morbidities and/or complications are not uncommon). The GDG felt that management of essential hypertension in primary care is a priority area given the perceived variation in management of early disease in a rural/primary care setting and the opportunity to spread best practice across the country drawing on the experience of the tertiary care centres operating in the major urban centres.

  In addition, screening and a public campaign to raise awareness of hypertension and encourage early diagnosis and treatment as well as prevention, were also identified as key priorities. However, given the restrictions in terms of resources and time, the GDG and technical teams decided to focus on an area where a significant degree of analysis had already been undertaken by NICE –i.e. pharmacological treatment. Prevention and health promotion can form separate initiatives following on from this pilot (see below).

- Scoping and developing the clinical question: The following clinical question was agreed upon: “Clinical and cost-effective pharmacological management of essential hypertension in adults presenting in a primary care setting in Jordan.” Treatment initiation with combination therapy (A+C vs. A+D) was discussed as an option for the adapted guideline given that this seems to be more

[1] In addition to the feedback from the Dead Sea workshop, in designing this pilot, we built on previous initiatives in the region such as the WB-funded methods for guideline development project Jordan Health Sector Reform Project – 2004).

consistent with current practice in Jordan, international guidelines and recently reported trials. However, the cost-effectiveness of this strategy is, as yet, unproven. It was also agreed that the guideline should consider the choice of first-line monotherapy and in particular the role of β-blockers as first line treatment in patients with no co-morbidities. The different treatment combinations to be analysed would be subject to available trial data, so clinical consensus would be required to derive the final recommendations during Phase II.

- Identification of data sources; Evidence on clinical and cost-effectiveness underpinning the NICE guideline on hypertension management (2006) was reviewed. There was discussion of major additional relevant trials published in the last 3 years (e.g. ACCOMPLISH trial) and of how these may affect the guideline recommendations, their application in the Jordanian setting and necessary adaptations. The availability of Jordan-specific data on cost inputs, resource use estimates and clinical effectiveness was also discussed and potential sources for these data identified. A list of data requirements for updating the clinical and economic analysis is given in Appendix C.

By the end of Day 3 the GDG had agreed on a clinical question of relevance to Jordan, identified major sources of additional information to ensure the guideline developed would be adapted to the Jordanian system.

e. *Allocation of workload across technical team:* A meeting with the technical teams of the UK and Jordan followed the end of the GDG. Tasks were allocated and an action plan developed. The Jordanian team led on retrieving data to inform the update of the economic analysis through interrogating relevant databases, interviews and focus groups with clinical and policy experts. The UK team led on reviewing evidence from recent clinical trials and adapting the NICE economic model for Jordan.

Phase II of the pilot including second visit and analytical work in Jordan and the UK

f. *Analytical work in Jordan:* A team of four experts drove the data collection in Jordan, which then informed the updated analysis of the clinical and economic evidence. Below we summarize the activities between the two visits and the challenges experienced in retrieving the necessary data.

In order to populate the economic model with data relevant to the Jordanian hypertensive population and healthcare system, the following parameters were needed:

- Annual CVD and non-CVD related mortality by gender and age strata

- Annual incidence among people with hypertension of primary CVD events (UA, MI, stroke and CVD-related death) by gender and age strata
- Annual incidence of secondary CVD events (UA, MI, heart failure, diabetes, stroke and CVD-related death) following previous CVD events
- Quality of life with and without the occurrence of CVD events
- Costs (drug costs, costs of hypertension management, costs of CVD event management); comprising information about resource utilisation and unit costs.

A literature review was conducted to identify relevant clinical, humanistic and economic data in Jordan or in similar Middle Eastern countries. Although some estimates were available, such as disease-specific mortality in the Jordanian population, other data were difficult to find[2]. Thus, given the limited time and resources available to prospectively collect the needed information, missing parameters were elicited from experts. A series of meetings were conducted with physicians from King Abdallah Hospital, Jordan University Hospital, Princess Basma Hospital and the Royal Medical Services.

A total of four physicians were able to provide the group with estimates. However, information was sparse, and physicians generally felt uncomfortable providing estimates. In particular, it was difficult to elicit values for the risk of cardiovascular events. The general consensus after meeting with the physicians was to use the incidence data from the UK. Physicians generally agreed that there was no reason to believe why international estimates of risk (and drug efficacy) were not applicable to the Jordanian hypertensive population.

Following these preliminary meetings, a focus group was arranged to elicit additional parameter values from physicians. A tool containing all required data elements was developed to facilitate elicitation. However, some challenges were faced in the conduct of the focus group meeting:

- Time and scheduling constraints limited the extent to which the physicians could be prepared for the meeting (e.g. for those that did not attend the first workshop, brief handouts or presentations given in advance about the MeTA initiative and how physician input would be used within an economic model)
- Very few physicians attended the meeting
- Those in attendance felt it was too difficult to provide estimates of cardiovascular risks, and reiterated the opinions of the physicians interviewed initially (that estimates from the UK model should be used)

[2] Estimates should be interpreted with care. For example, mortality estimates differed according to reporting sources (Department of Statistics versus the Ministry of Health) as a result of differences in the procedure of updating death records.

- Physicians also felt hesitant about providing quality of life and resource use estimates, since they felt it was difficult to generalize from their individual experiences with patients. Nevertheless, preliminary quality of life estimates and resource utilization scenarios were elicited for each CVD event Unit cost data for antihypertensive medications and for services used to diagnose and treat cardiovascular disease were then obtained in order to project the approximate cost of each CVD event. The costs of medications were based on World Health Organisation 'defined daily doses' (DDDs).

g. *Analytical work in the UK*: Using the feedback from the first GDG and the data retrieved by the Jordanian team, the clinical evidence review and economic analysis were updated to inform the Jordanian guideline.

   The clinical evidence was updated by identifying any known major trials that had been published since the last update of the NICE hypertension guideline. Although the update guideline focused on studies looking at monotherapy (head-to-head drug comparisons) for first-line treatment, it was agreed by the GDG during phase I of the Jordan pilot, to also look for trials comparing first-line combination therapies (such as ACCOMPLISH). All trials identified were critically appraised for their quality and robustness of design, and the results were summarised using GRADE (modified version used by NICE).

   The NICE economic model was adapted for use in the Jordanian context:

   - **o** Firstly, its presentation was improved to enable easy handover of the model for later development and use by Jordanian economists. This included simplifying the data input screens, as well as taking out some redundant parts of the model (for example, the facility to adjust the results for different ethnic groups).
   - **o** Secondly, the model was adapted to allow estimation of the cost-effectiveness of the combination treatments compared in the ACCOMPLISH trial, in addition to the comparison of first-line treatments in the NICE clinical guideline.
   - **o** Thirdly, the data obtained by the Jordanian team was entered into the model.
   - **o** Fourthly, the model was prepared to allow 'live' exploration of important uncertainties over model parameters with the Jordanian technical team and with the GDG if desired.

h. *Guideline adaptation (2nd GDG)*: During the second GDG meeting, a number of activities took place, leading to the development of an evidence-based clinical algorithm for the pharmacological treatment of hypertension:

- During Day 1 of the second visit, the UK and Jordanian technical teams went through the literature review and economic analysis. The model structure and individual model inputs were discussed and amended where necessary to reflect the latest available information. Areas of uncertainty were discussed and two major types of input were identified for checking and further elicitation by the GDG: quality of life information and resource use/common practice patterns of management of hypertensive patients following complications.

- During Day 2, the review of clinical evidence from the NICE guideline and subsequent major clinical studies were presented and discussed. The GDG were reminded of the structure of the economic model, and reviewed the Jordanian data elicited from the focus group, which were then amended based on the GDG's feedback. Weaknesses of the evidence base, key uncertainties and evidence gaps to which the model was most sensitive were identified and discussed further. Additional information on unit costs for MoH providers was retrieved. The focus group's utility values were revised by the GDG and checked against UK population level values – the two were very similar. The GDG also checked and revised the list of medications and dosages, and the assumptions about resource use following cardiovascular events.

- During the second day, a patient treated for hypertension in Jordan presented his experience to the GDG, which informed a discussion of the challenges of managing the disease in the Jordanian system. Representatives of the payers/insurers were also present.

- During Day 3 the model results were presented to the group. The evidence was then translated into recommendations in the form of an algorithm (see Appendix D), taking account of clinical opinion, and additional local context-specific factors not included in the reviews and economic analysis. The GDG had the opportunity to review and comment on the draft algorithm prior to finalisation. This was followed by a discussion of implementation and next steps. A number of possible steps were identified. The key amongst these are listed below:

- Dissemination workshop to raise awareness amongst stakeholders and receive feedback
- Official approval of the guideline by the MoH
- Incorporation into implementation strategy led by MeTA Jordan, which may include additional technical training; awareness raising and budgetary impact analysis to inform procurement
- Linkage with procurement and rational drug use of medicines

- More research into Jordanian epidemiological parameters; utilities; unit costs and baseline data on prescribing practices.

Additional possible activities discussed include:

- Establishing specialist society –e.g. Jordanian Hypertension Society- and an affiliated patient/service user society to promote awareness amongst patients and the general population
- Launching a national champion/national campaign –e.g. Know your numbers
- Beginning of streamlined process to develop standards for screening, primary prevention, diagnosis, non-pharmacological treatment and follow-up for CVD and other chronic diseases (e.g. diabetes)
- One or more academic publications to raise awareness amongst policy makers globally and show-case Jordan as an example of middle-income country with a commitment to evidence-based policy-making
- Presentations in national and international conferences such as the International Society for Hypertension
- Development of lay version of GL accessible to patients
- Sharing with other MeTA countries within the network.

NICE International can contribute to some of these activities, especially with regard to help inform an implementation strategy.

Pilot Deliverables

- Evidence informed clinical algorithm for the pharmacological management of essential hypertension in adults in primary care in Jordan *delivered*
- Economic model[3] adapted to the Jordanian setting allowing future adaptation and further analyses using Jordanian input costs, utilities (elicited) and common management practices reflecting the Jordanian system *delivered*
- Pilot report describing the process and methods followed to deliver on the final products *delivered*

[3] Licensed to MeTA Jordan for non-commercial use in Jordan and the MeTA pilot network

- Training and improved understanding (technical, procedural and policy-related) and awareness (amongst clinicians and policy makers) of the potential benefits of Jordanian guideline development *delivered*

In addition, the UK and Jordanian technical and project teams will aim jointly to produce and publish a peer-reviewed paper in an international journal describing the processes and methods followed during this pilot, highlighting the capacity, evidence and process-related challenges faced by the team and offering lessons learned so that the overall approach can be improved in the future.

The team

The NICE International team comprises Jordanian and UK experts, including clinicians, pharmacists, systematic reviewers and health economists as well as healthcare professionals with frontline expertise in the clinical area selected. In addition, throughout the process, we drew heavily on the expertise of a broad range of stakeholders on the Guideline Development Group.

Follow-up visits and additional activities

Subject to the level of interest of Jordanian stakeholders and to additional funding, a number of activities to support the uptake of the recommendations; strengthen the technical skills of local experts and encourage the development of evidence based recommendations in Jordan and other interested MeTA countries, can be pursued:

i. Pilot to assess how a guideline-based budget impact analysis using local baseline data can inform procurement and forecasting and link with the rational drug list
ii. Further technical training for local technical and clinical experts to build a core competencies to reproduce and improve the piloted approach to other disease areas in Jordan (e.g. diabetes) and across the MeTA network
iii. Process support including consultation processes, patient and public engagement, conflict of interest management and quality assurance, review and update mechanisms
iv. Implementation training and support including national initiatives such as the setting up of a Jordanian Hypertension Society and an affiliated patient organisation and broad dissemination of the product through formal launch event and other awareness raising campaigns (e.g. 'Know you numbers' in the UK)
v. Dissemination workshops across interested MeTA countries, run in collaboration with MeTA Jordan

Appendix A: Membership of the Guideline Development Group

Name	Institution	Specialty
Dr Taher Abu El Samen	HHC	Secretary General, High Health Council/ Chair of MeTA Council
Dr Ahmad Al Barmawi*	HI/ MOH	MD, DG HI Directorate
Dr. Akram Al-Saleh	JUH	Cardiologist
Dr. Ayman Wahbeh	JUH	Internist/Nephrology
Dr. Khawlah Abu-Hamour	JUH	Director, Pharmacy Department
Dr. Lama Hmoud	MOH	Director , Clinical Pharmacy Department
Taher Batah	JUH	Nurse
Dr. Na'el Al-Shobaki	KAUH	Cardiologist
Dr. Yousef Wardat	KAUH	Family Medicine
Dr. Housni Sadeq	RMS	Internist
Dr. Hatem Salahen	RMS	Cardiologist
B. G. Dr. Waffa Nsour	RMS	Director of Pharmacy Department
M. G. Dr. Reham Al-Nazeef	RMS	Director of Supply and Purchasing Department
Dr. Abeer Rabaya'a	MeTA	MeTA National Secretariat
Dr. Dana Darwish	Petra University	Clinical Pharmacy
Dr. Michael Halassah	MOH	Internist
Dr. Maysoon Al-Kelani	MOH	Family Medicine
Dr. Mounir Abu Helaleh	KHCC	Cancer Control Programme

Dr. Lubna Qousous	JFDA/RDU	Pharmacist
Dr. Ali Al Ibrahimi	Department of Social Security	Assistant Director/ Health Affairs
Dr. Adeeb Masrogi	Department of Social Security	Physician
Dr. Ikhlas Jaber	MOH/Prince Hamzeh Hospital	Director of Pharmacy
Dr. Njoud Fares	MOH/Prince Hamzeh Hospital	Pharmacist
Dr. Samia Saad	MeTA	MeTA Consultant
Dr. Salah Gammouh	WHO	Technical Consultant
Mr. Fehmi Al Osta*	Patient Representative	HHC

* GDG 2 only

Appendix B: Membership of Technical Team

Jordan

Dr Ayman Momani – Co-founder & CEO, PharmaNet

Dr Ibrahim Al-Abbadi - Scientific Research Documentation Office Manager, University of Jordan

Dr Nour Obeidat - Head, Center for Health Economics & Outcomes Research, King Hussein Institute for Biotechnology and Cancer

Dr Lara Qatami - Assistant Director for Strategic affairs, King Hussein Cancer Center

Dr Rania Bader – Pharmaceutical Policy Consultant, Department for International Development MeTA project.

UK

Dr Adrian Stanley - Consultant Physician in Cardiovascular Medicine, University Hospitals of Leicester NHS Trust

Dr Kalipso Chalkidou – Director, NICE International

Dr Joanne Lord – Reader in Health Economics, Brunel University

Dr Rachel O'Mahony – Research Fellow and Senior Research Fellow in Guideline Development, National Clinical Guidelines Centre for Acute and Chronic Conditions

Mr Derek Cutler – Project Manager for Jordanian pilot, NICE International

Appendix C: Jordan data requirements

- Estimates of treatment effects (from the updated systematic review)

Epidemiological parameters:

- Incidence of CVD-related deaths, non-fatal CVD events (MI, stroke, unstable angina), and new-onset diabetes and heart failure in a hypertensive population without prior CVD or diabetes (by age)
- Incidence of CVD-related deaths, non-fatal CVD events (MI, stroke, unstable angina), and new-onset diabetes and heart failure in a population with prior CVD or diabetes (by age)
- Mortality rates in the general population - CVD related and general (by age)

Costs:

- Costs of prescribed antihypertensive drug treatments in Jordan (branded and generics),
- WHO Defined Daily Doses for antihypertensive medications

Use of health services to prescribe antihypertensive medications, including follow-up and any tests for contraindications or side effects • Use of health services to diagnose and treat non-fatal MI, stroke, unstable angina, diabetes and heart failure (for first and subsequent years)

- Unit costs of CVD services to Jordanian public payers (Ministry of Health tariff for RMS providers).

Utilities:

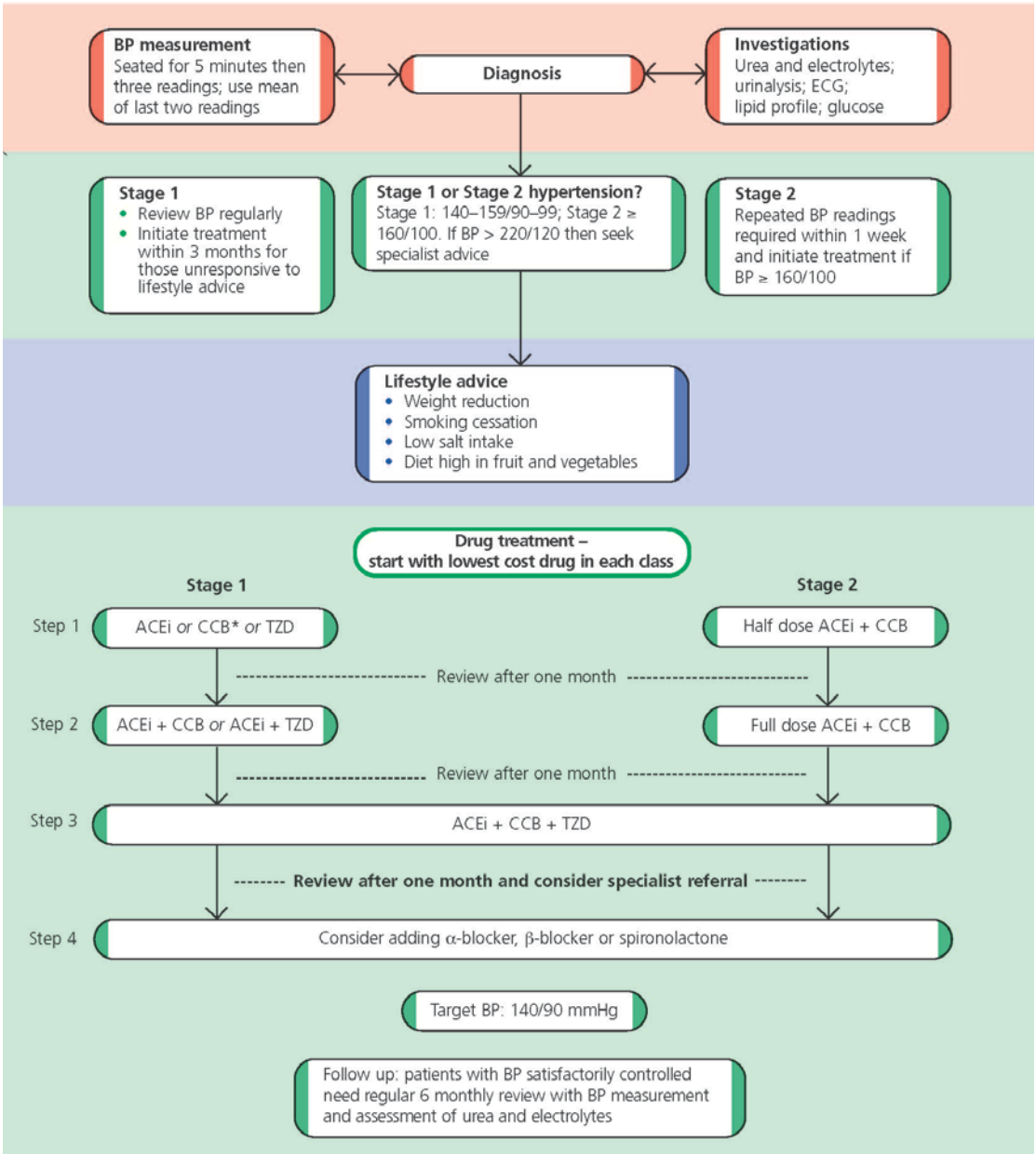
•Mean quality of life (utility) in the general population (by age)
•Relative utility reductions due to CVD events, diabetes and heart failure (year one and subsequent)
•Relative utility reductions due to side effects from antihypertensive drugs
•CEA thresholds based on WHO guidelines:
http://www.who.int/choice/costs/CER_thresholds/en/index.html

Cost impact analysis:

•Prevalence of hypertension in the population - based on a definition of >140/90
•Distribution of CVD risk in people with (untreated) hypertension (in case GDG wishes to recommend treatment thresholds based on CVD risk)
•Current prescribing levels and costs for antihypertensive medications available in Jordan
•Expected uptake (% compliance with guideline recommendations)

Appendix D- Final guideline algorithm

Guideline for the management of newly diagnosed uncomplicated hypertension in Jordanian primary care



ACEi = angiotensin converting enzyme inhibitor (consider angiotensin-II receptor blocker (ARB) if ACEi intolerant)
CCB = calcium-channel blocker; *CCB is preferable for patients aged over 60 years
TZD = thiazide-type diuretic

A project delivered by NICE International with sponsorship from the World Bank and the UK Department of Health and with the support of the Jordan Medicines Transparency Alliance.

Implementing the guideline

The Medicines Transparency Alliance Jordan is leading on the implementation of this guideline (see www.medicinestransparency.org/meta-countries/jordan).

Key steps:

- Multi-stakeholder workshop to raise awareness and get feedback
- Ministry of Health approval
- Establish baseline practice and monitor uptake
- Link with public sector procurement strategy and rational drug use
- Launch national awareness campaign for healthcare professionals and patients (for example, Know Your Numbers! – see www.bpassoc.org.uk/microsites/kyn)
- Set up process for review and update of guideline.

More work needed...

- Prospective cohort studies to establish key epidemiological parameters in Jordan, including incidence of both hypertension and cardiovascular events in hypertensive patients
- Population surveys to establish the quality of life values for the Jordanian population
- Reliable sources for unit costs of drugs, clinical interventions and services offered in the various sectors (MoH, RMS, university, private)
- Regional and national audit to establish baseline data on resource use and prescribing patterns
- Explore the use of electronic medical records systems to collect data.