

Dementia diagnostics-treatment-care

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This evidence brief provides a summary of management of dementia, including diagnostics and follow-up care, drugs, and support of care givers, with a particular emphasis on parameters used in *FairChoices: DCP Analytics Tool* (FairChoices).

Table 1: Summary of model parameters and values used in FairChoices – DCP Analytics Tool, more details about assumptions and interventions in text after this table

Population:	All prevalent cases of dementia, both genders, all ages (Dw=0.14 in average)
Intervention	Diagnostics and follow-up care Drugs for dementia <ul style="list-style-type: none"> – Cholinesterase inhibitors (Donepezil, Galantamine, Rivastigmine) – SSRIs (Citalopram, Fluoxetine, Sertraline) – Antipsychotics (Aripiprazole, Risperidone, Haloperidol) Supporting dementia caregivers – 5% reduction of disability (improved HRQoL)
Comparator	No intervention
Outcome	Disability weight (health related quality of life)
Effect	Diagnostics: 0% effect Drugs for dementia <ul style="list-style-type: none"> – Cholinesterase inhibitors: 20% reduced disability (improved HRQoL) – SSRIs: 20% reduction of disability (improved HRQoL) – Antipsychotics 5% reduction of disability (improved HRQoL) Supporting dementia caregivers: 5% reduction of disability (improved HRQoL)
Unit cost**	Diagnostics: 2.1 US\$ LIC; 5.9 US\$ LMIC Drugs for dementia <ul style="list-style-type: none"> – Cholinesterase inhibitors: 624 US\$ LIC; 630 US\$ LMIC – SSRIs: 7.2 US\$ LIC; 13.9 US\$ LMIC – Antipsychotics 4.3 US\$ LIC; 11.0 US\$ LMIC Supporting dementia caregivers; 0.4 US\$ LIC; 0.9 US\$ LMIC

* Dw=disability weight, HRQoL=Health Related Quality of Life, LIC=Low Income Country, LMIC=Low-Middle Income Country

** Annual cost per treated patient, 2021 currency, see cost assumptions and calculations below

Description of condition and intervention

Dementia is a progressive syndrome which is characterized as a deterioration that cannot be attributed to a consequence of normal aging and interferes with the self-sufficiency of a patient in everyday life functioning. Dementia is defined as a decline or loss in cognitive functioning on more than one cognitive domain, which is typically memory and another domain, such as executive functioning, attention span, or language [43]. Dementia is an umbrella term for different types of conditions, such as the most known variants of dementia, namely Alzheimer's disease, or vascular dementia, but dementia can also result from an underlying pathology, such as Huntington's disease, Lewy Body dementia, or Creutzfeldt-Jakob disease, or as a consequence of neurocognitive conditions that are associated with HIV (see Table 1 in the appendix) (Howlett, 2012).

The cause of dementia is different in every type, but common risk factors are old age, cardiovascular risk factors (such as diabetes, high cholesterol, or heart diseases), brain injuries or genetics. As the disease progresses it leads to social behavioral changes, such as agitation, feeling more emotional, or not being able to control impulses (WHO).

The WHO has estimated that there are around 47.5 million people globally that suffer from a form of dementia, with an incidence of 7.7 million cases a year (WHO). In sub-Saharan Africa it was estimated that 2.13 million people were diagnosed with dementia in 2015, a number which is projected to reach 7.62 million in 2050 due to an expected increase of cases in Eastern and Central Africa, mainly resulting from an aging population (Guerchet et al., 2017). Based on GBD 2019 data, we assume that disability weight is in average 0.14 for dementia. However, this varies by severity (Mild: 0.069; Moderate: 0.377; Severe: 0.449, (Neumann et al., 1999)) and since the majority of patients have mild dementia we see a low value of the average disability weight.

The global societal costs of dementia are estimated to be around \$820 billion (see Table 2 in the appendix) (Dotchin et al., 2014). Prince et al. (2015) demonstrate that the costs can be explained by direct and indirect health costs associated with dementia, such as the use of primary health care services or institutionalization, but also the costs for loss of the ability to work for the patients. The costs also include costs from family members caring for a patient, due to low productivity or absenteeism from work (Prince et al., 2015; Prince et al., 2016). These costs add up to high financial consequences for families involved, especially in the low- and low-middle income countries (LICs/LMICs) (GBD Dementia collaborators., 2019; Prince et al., 2016). Furthermore, the expectation is that these costs will increase tremendously as a result of the increasing burden of disease due to aging populations.

International guidelines for dementia

Organization	Guideline	Applicability in LIC & Lower MIC settings
WHO (2017)	Risk reduction of cognitive decline and dementia	✓
WHO (2021)	Evidence-based recommendations for management of dementia in non-specialized health settings	✓
WHO (2018)	Towards a dementia plan: a WHO guide	✓
Alzheimer's disease international (2017)	Dementia in sub-Saharan Africa Challenges and opportunities	✓

Source: Alzheimer's Disease International (2017), World Health Organization 2017, 2018, 2021

1. Diagnostics and follow-up primary care

Receiving a dementia diagnosis in an early phase of the condition requires a mental, physical, and social examination. Diagnosis can be supported by neuroimaging, such as an MRI, or identifying biomarkers through cerebrospinal fluid through lumbar puncture, also known as spinal tap, although this is generally not performed in LLMIC settings (Howlett, 2012). Additional neuropsychological screening or testing can provide insight in the reduced function of any of the cognitive domains, such as memory, attention span or language. However, translations of diagnostic- or screening tests are not always available into the patient's native language and may therefore not always applicable to LLMIC settings. Secondly, not all neuropsychological tests have been validated in LLMICs (Guerchet et al., 2017). Further problems that contribute to underdiagnosis include limited health literacy, limited access to health care services and lastly stigma (Maestre, 2012).

Diagnosis in LLMICs often occurs through the process of clinical diagnosis, where health personnel base their diagnosis not on medical tests but on symptom description of the condition and daily functioning. Therefore, the diagnosis is usually made by diagnostic interviews with patient and a close family member, reviewing the medical history of the patient, neuropsychological screening, and testing. Often the indication from close family members or partners that someone can perform so-called activities of daily living (ADL) and therefore are no longer self-sufficient is indicative for dementia (Guerchet et al., 2017).

Dementia decline is often measured as progression on the MMSE. Early screening with the Mini Mental State Exam (MMSE) can identify individuals with dementia earlier on, and subsequently,

adequate care can be provided (e.g. an nutritional checkup, weight, height, examination of vital signs or a possible early start on cholinesterase inhibitors). This often results in delayed institutionalization, which has positive effects on the health care system, family and community, however due to the limitations listed above, a timely diagnosis is not always obtainable.

Follow up and primary care of patients is important in order to assess the health status, as impaired cognition might result in not addressing other coexisting illnesses in an adequate manner. Because of the dementia, patients might not remember to take their medication, take too much medication or forget to eat and therefore lose weight or have severe nutritional deficits. An adequate follow-up can aim to prevent this by providing check-ups on a patient's health status. Primary care might also slow down vascular risk factors that can progress dementia even further (Prince et al., 2015; Prince et al., 2016).

An American systematic review shows that patients that suffer from dementia have a better quality of life when they are still able to perform ADL-tasks, are able to perform pleasant activities, are in good health and have good mobility and mood, and naturally a preservation of cognitive functions (Logsdon et al., 2007). However, studies on the quality of life in LLMICs are scarce.

In dementia care, the focus is placed on the role of prevention through improving lifestyle factors and early diagnosis. Early diagnosis provides room for better management of dementia, providing psychoeducation and support for caregivers in a sustainable way (WHO, 2015). Early diagnosis could lead to reduced costs due to better management, however, early diagnosis could be a negative influence on social and psychological factors.

2. Drug treatment

There are no effective pharmacological treatments to prevent or treat dementia to date. Many studies have been conducted to assess the efficacy of cholinesterase inhibitors (for example, donepezil, rivastigmine or galantamine) to impede or treat Alzheimer's disease, however no evidence is available in LLMIC settings (Prince et al., 2015). Secondly, these medications are not on the list of essential medicines. Pharmacological treatment for symptoms is sometimes given in the form of SSRIs or antipsychotics to help with the agitation, anxiety, psychosis, and behavioral symptoms that can occur in patients with dementia (Patel et al., 2016). Risperidone and haloperidol are on the list of essential medicines. Psychological treatments or interventions are given to patients to help reduce the behavioral symptoms (Cross et al., 2018).

Baseline coverage is currently set at 5%/8% for SSRIs and antipsychotics and 0% for cholinesterase inhibitors in LIC/LMIC settings.

Dementia typically leads to a reduction of 3-4 (mean 3.5) points on the MMSE per year. Drug treatment can slow this reduction with 1 –2 (mean 1.5) points a year (Bullock et al., 2005). Hence, patients benefit from early treatment.

3. Supporting dementia caregivers

The progressive nature of the disease leads to a need for constant supervision from caregivers, and makes a dementia patient highly dependent for help on daily tasks. Caregivers are often family members, in particular the patient's children, and caregiving tasks can be shared in between members of the household. In LLMIC settings, caregiving at home is more common than professional care as the family support systems may be better, larger and more feasible (Gupta et al., 2012). It is estimated that 58% of the costs of dementia in LIC settings and 65% in middle-income countries are because of all costs related to informal care (Wimo 2013). The 2010 World Alzheimer Report (2010) assumes that in East sub-Saharan Africa, informal caregivers (81% female, 41% of the cases this equals a spouse) spend 3.6 hours per day on activity of daily living (ADL) tasks and 2.6 hours per day on supervising the dementia patient.

The term "caregiver burden" entails the physical, mental and socio-economic consequences that occur from providing care for a loved one (Zarit et al., 1986). Dementia carries a lot of stigma, that also extends to caregivers and causes stress (Dotchkin, 2014).

Interventions targeting caregivers consist of psycho-education to advise about the disease and its symptoms, psychological therapy such as cognitive behavioral therapy or counseling. Interventions can serve as guidelines in care taking, caregiver support or respite (emergency) care, or a combination. Many of the caregiver interventions focus on reducing stress and depressive feelings to prevent the caregiver from being overburdened, ultimately resulting in better care for the patient (Patel et al., 2016). Cognitive behavioural therapy has the highest impact. It is important that these programs are implemented from a horizontal, health system approach in a community program.

As dementia is not always accurately diagnosed in LLMIC settings, strategies that could lead to an improved quality of life for patient and caregiver, such as home optimization strategies in an earlier stage of dementia, are not among the possibilities. These home-modifications can postpone institutionalization and allow for as much independence in activities of daily living (ADL). However, institutionalization in LLMICs is not always a possibility either.

Not much evidence is available on caregiving in sub-Saharan Africa, yet the limited evidence is contested, for example due to lack of randomized studies, studies in appropriate settings, or

studies using flawed methodology. A study in Nigeria showed that the levels of stress that accompany the provision of care is just as high as the levels of stress in HIC (Prince et al., 2004). Results from a community-based study in the Hai district in Tanzania implied that caring for dementia patients does not carry a high burden, as the symptoms in an early phase of the disease are often attributed to the normal ageing process (Logsdon et al., 2013). A follow-up study showed that taking care of patients with neurodegenerative disorders leads mild to high levels of burden for the caregivers, especially when there is no professional support, options for institutionalization, or limited money and resources (Dotchkin et al., 2014). Providing care for dementia patients impacts the quality of life of both the patient and the caregiver and increases direct and indirect household-related costs because of medical expenses or missing out on income as a result of absenteeism from work. (Patel et al., 2016).

In a randomized controlled trial, a multicomponent intervention was assessed in White/Caucasian, Hispanic/Latino, or Black/Afro-American caregivers of dementia and Parkinson patients when compared to a control group. The results show that the intervention, that focused on depression, care burden, social support, self-care and patient problem behaviours, improves the quality of life of caregivers for the white/Caucasian group and the Hispanic/Latino groups only. In the black/Afro American group a significant increase in Health-Related Quality of Life (HRQoL) was observed when the caregivers were the patient's spouse (results in table 2). However, the limitations to this study are that there is a the relatively short (6-month, one time only) follow-up period (Belle et al., 2006), and it is focused on differences in the USA only.

Table 2: HRQoL impact of having family/spouse as caregiver.

White/Caucasian	Coeff, -0.2 (CI, -0.4 to 0.0)	P<0.032
Hispanic/Latino	Coeff, -0.3 (95%CI, -0.5 to -0.1)	P<0.001
Black/African-American	Coeff, -0.1 (CI, -0.3 to 0.1)	P=0.23
Black/African-American intervention x spouse interaction	-0.5 (CI, -0.9 to -0.1)	P=0.008

In a systematic review, the authors compiled a list of 10 themes that came up during qualitative analysis to estimate which factors that matter the most with respect to the quality of life for caregivers of dementia patients (Farina et al. 2017):

1. Demographics
2. Carer emotional wellbeing
3. Carer-patient relationship
4. Support received
5. Dementia characteristics
6. Carer independence
7. Demands of caring
8. Carer self-efficacy
9. Carer health
10. Future

A qualitative study in Uganda describes the impact of caring on informal caregivers that extends to a physical, financial and social burden (Ainamani 2020). The recommendations are to provide and extend support services, such as groups, counselling options, and campaigns targeting knowledge on dementia, reducing stigma and creating a better understanding of the caregiver burden.

Baseline coverage for interventions targeting caregivers is currently set to 5%/8% for LIC/LMIC settings in FairChoices as health care workers are assumed to not be aware of this intervention.

Intervention attributes

Type of interventions

1. Diagnostic, 2. chronic management care, 3. health promotion

Delivery platform

1. Hospital, 2. Hospital/health centres, 3. community

Equity

In addition to considerations like cost-effectiveness and health systems factors, dimensions of equity can be relevant for priority setting. The opportunity for a long and healthy life varies according to the severity of a health condition that individuals might have, so there are inequities in individuals' opportunities for long and healthy lives based on the health conditions they face. Metrics used to estimate the severity of illness at an individual level can be used to help prioritize those with less opportunity for lifetime health. FairChoices: DCP Analytics Tool uses Health adjusted age of death (HAAD), which is a metric that estimates the number of years lived from birth to death, discounting years lived with disability. A high HAAD thus represents a disease less severe in terms of lifetime health loss, while a low HAAD represents a disease that is severe on average, causing early death or a long period of severe disability. It is also possible to estimate the distribution of HAAD across individuals with a health condition. FairChoices shows for each intervention an average HAAD value of the conditions that are affected by respective interventions that have health effects. Additionally, a plot shows HAAD values for around 290 conditions (Johansson KA et al 2020).

Time dependence

Moderate level of urgency and treatment outcomes will not be highly affected by some days of delay.

Population in need of interventions

All prevalent cases would benefit from diagnosis of dementia and follow-up care.

All individuals diagnosed with dementia from psychiatric symptoms can benefit from drug treatment with antipsychotics.

The caregiver intervention is targeted at all caregivers that take care of a dementia patient. This benefits both the caregivers as well as the dementia patients.

Disease stage addressed

The disease stage addressed is the moment of diagnosis of dementia, which is often assessed when the patient has reached a level of reduced self-sufficiency, and the care patients receive afterwards. For drug treatment, Treatment is initiated in diagnosed individuals, or after experiencing psychiatric symptoms that can occur with dementia. GBD condition "*Alzheimer's disease and other dementias*" is used to match with country specific epi data input.

Intervention effectiveness and safety

1. Diagnostics and follow-up: Patients experience no direct health benefit from a dementia diagnosis, but it comes at a cost. During follow up, patients receive weight, height and blood pressure measurements. However, dementia diagnosis is treated as a prerequisite for further interventions. Baseline coverage set at 5% in LIC and 8% in LMIC setting.
2. Drug treatment: The effects of the cholinesterase inhibitors donepezil, rivastigmine, and galantamine will be assessed, as well as the antipsychotic drug risperidone. Baseline coverage is currently set at 5%/8% for antipsychotics, 25% for SSRIs and 0% for cholinesterase inhibitors in LIC/LMIC settings.
3. Supporting caregivers: Baseline coverage is currently set at 5%/8% in LIC/LMIC settings. If community health workers are not aware of the condition, caregivers currently receive no support.

Cholinesterase inhibitors

The cholinesterase inhibitors in this model were selected by selecting the ones that are most frequently assessed in literature reviews and meta-analyses and have proven to show a degree of efficacy as well as are considered safe.

Antipsychotics

Antipsychotics are sometimes used in the treatment of dementia as a last resort type of drug treatment. However, as they pose many side effects and have a small effect size in general, they should be considered last in the pharmacological treatment. The drugs haloperidol, aripiprazole and risperidone are listed below. Other antipsychotics, like olanzapine and quetiapine were excluded as their effectivity and safety does not surpass the effects of the previously mentioned options. A meta-analysis of antipsychotics shows that aripiprazole is associated with improvement of NPI, BPRS and CMAI scores and is safer, compared to risperidone (Yunusa et al., 2019).

SSRIS

To treat the behavioural symptoms of dementia, SSRIs can be used. Popular choices are citalopram, fluoxetine and sertraline. In this model we use Fluoxetine and sertraline, as no costing information was available for citalopram.

Supporting caregivers

Determining the effectiveness of caregiver interventions is complex as this has an effect on both the patients and caregivers simultaneously. Outcomes for the caregivers however, are mainly non-health benefits for the caregivers, such as outcomes in quality of life, and depends on the disease stage. Indirect benefits for caregivers are not analysed in FairChoices. The quality of life for the caregivers will indirectly affect the patients and the effect measure was set to 5% reduction of disability weight of the patient (assumption, no evidence identified).

A summary of the assumed health effects of the dementia interventions (with detailed overview of findings from literature and rationale for these assumptions are provided in table 3):

Diagnostics: 0% effect

Drugs for dementia

- Cholinesterase inhibitors: 20% reduction of disability / improvement of HRQoL
- SSRIs: 20% reduction of disability / improvement of HRQoL
- Antipsychotics 5% reduction of disability / improvement of HRQoL

Supporting dementia caregivers – 5% reduction of disability / improvement of HRQoL

Table 3: Population and effectiveness of interventions for dementia

Category	Model parameter	Notes
Treated population Gender Age	All patients All caregivers Both 60-99 18-99	 For dementia patients For dementia caregivers
Affected Population	Prevalent cases	
Intervention	Drug treatment for dementia patients	Both disease moderators & antipsychotics
Comparison	Placebo	
Baseline disability dementia	Mild: 0.069 Moderate: 0.377 Severe: 0.449	(Neumann et al., 1999.)

Mortality Reduction (RRR)	Not reported	
Disability Reduction (RRR) of atypical antipsychotics	Between -0,32 / -1,84	Based on improved performance on 4 different rating scales compared to placebo (Ma et al., 2014)
Diagnosis and follow up	0	Assumed 0 due to no direct health benefits
<u>Cholinesterase inhibitors</u>		
Donepezil	NPI Mean difference – 1,45 95% CI –2,70 to – 0,20 MMSE: Mean difference 1.05, 95% CI 0.73 to 1.37	Jin & Liu, 2019 After 26 weeks the drug is associated with better cognitive outcomes compared to a placebo (Birks et al., 2018)
Galantamine	NPI Mean difference – 1,80 95% CI –3,29 to – 0,32 Placebo: -2,14 (4,34) Drug: -1,41 (4,05)	Jin & Liu, 2019 Worsening on MMSE in 24 months: P<0,001 (Hager et al., 2014)
Rivastigmine	NPI Mean difference – 1,09 95% CI –2,89 to 0,67 (not significant!) MMSE: Mean difference 0.74, 95% CI 0,52 to 0,97	After 26 weeks the drug is associated with better cognitive outcomes compared to placebo (Birks et al., 2015)
<u>Antipsychotics</u>		
Aripiprazole	NPI Mean difference – 3,65 95% CI –6,92 to – 0,42 NPI: standardized mean difference -0,17, 95% CI – 0,31 to –0,02 BPRS: standardized mean difference 0,20 95% CI – 0,35 to –0,05 CMAI standardized mean difference -0,30 95% CI – 0,55 to - 0,05	Jin & Liu, 2019 Based on scores compared to placebo (Yunusa et al., 2019) Standardized mean difference <0,4 small effect size

Risperidone	NPI Mean difference – 3,20 95% CI –6,08 to – 0,31 CMAI standardized mean difference -0,26 95% CI – 0,37 to- -0,15	Jin & Liu, 2019 Compared to scores with placebo (Yunusa et al., 2019)
Haloperidol	NPI Mean difference – 3,44 95% CI –7,39 to – 0,40	Jin & Liu, 2019
Atypical antidepressants (SSRIs)		
Citalopram	mean difference MD, - 0.89, 95% CI, -1.22 to - 0.57	Agitation only - no costing information available
Fluoxetine	MMSE MD = 1.16, 95% CI: 0.41–1.90, P = 0.002	Xie et al., 2019
Sertraline		No costing information available
<i>Caregivers of dementia patients</i>		
Effect caregivers	No studies identified	Assumed to have similar efficacy as antipsychotics

Effectiveness Cholinesterase inhibitors

MMSE mean difference score

The effectiveness of cholinesterase inhibitors is measured on by reduction of points on the screening test Mini Mental State Exam (MMSE). The test has a maximum of 30 points that equals full, unimpaired cognition. A score between 25-30 would therefore be seen as no cognitive impairment. A score of 21-24 points can indicate mild cognitive impairment/mild dementia, between 10-20 points would equvalate moderate dementia and 9 or less points towards severe cognitive impairment. To determine the efficacy of the drugs, the following disability weights were used (Salomon et al., 2015):

Dementia: non 0.0 MMSE 25-30

Dementia: mild 0.069 (0.046-0.099)
MMSE 21-24

Dementia: moderate 0.377 (0.252-0.508)
MMSE 10-20

Dementia: severe 0.449 (0.304-0.595)

MMSE <9

Henceforth it was calculated that 1 point difference on the MMSE corresponds to $0.45/(25-9)=0.028$ in added disability.

Effectiveness antipsychotic effects based on NPI scores
NPI mean difference score

The Neuropsychiatric Inventory (NPI) was developed to screen behavior (such as agitation, hallucinations, sleep or anxiety) on the dementia spectrum and is to be filled out by the caregivers of a dementia patient. A sum score is given between by adding the 10 domain scores and ranges between 0-144 points. If the caregiver provides a positive answer on any of the behaviours, they are asked to score both the intensity and frequency on a score from 1-4. The multiplication of the intensity and frequency scores equals the domain score.

Non-health benefits:

These interventions are important because dementia treatment includes individual benefits, yet also provides benefits in broader perspective towards family members and society.

Diagnosis:

- More clinical benefits though timely treatment can improve the quality of life of patients and families
- Early diagnosis can provide for a good overview of future perspective.
- Patients have the right to know their diagnosis (ethically)
- Increased knowledge on disease through increased awareness early on

Drug treatment:

- Delay in clinical symptoms results in less burden for health personnel
- Improved quality of care resulting from diseased burden
- Delayed institutionalization
- Higher patient quality of life
- Higher quality of life for family members
- More societal participation
- Longer stable productivity of family members during the delay
- Lower indirect costs associated with the disease

Caregivers:

- Reduction of caregivers stress
- Increased productivity if caretaking becomes less demanding, resulting in an increased income
- Increased quality of life for patients

- Less strain on the workforce as patients require less professional help
- Consequences for social participation
- Increased perceived life control

Need for future research

Long term-controlled design studies with sufficient power and follow-up period needed to estimate the effect of dementia interventions.

Intervention Cost

For an elaborate explanation of the interventions, see description of condition and interventions.

Human resource unit cost

The time that should be spent per health professional per patient suffering from dementia, including the estimated time health care professionals spend on caregivers can be found in Table 3. The salaries of the health care workers can be found in table 4. The costs per minute for LIC are averaged between the salaries of Ethiopian health workers and Malawian health workers.

Table 4: Human resource component for the dementia interventions

Human resources	Number of visits	Time per visit (minutes)	Total time per case
Diagnosis			
Neurologist	1	30	30
Nurse	1	10	10
Follow up			
Neurologist	3	15	45
Nurse	3	10	30
Drug treatment			
Neurologist	4	10	40
Nurse	4	15	60
Supporting caregivers of dementia patients			
Community health worker	3	15	45

Table 5: Salaries health care personnel LIC / LMIC settings

	Cost per minute Ethiopia	Cost per minute Malawi	Cost per minute Tanzania	Cost per minute LIC (average)	Cost per minute LMIC (Tanzania)
Neurologist	0,060	0,064	0,178	0,062	0,178
Pharmacists	0,024	0,028	0,070	0,026	0,070
Medical doctor	0,047	0,044	0,131	0,045	0,131
Nurse	0,019	0,020	0,054	0,020	0,054
Community health worker	0,014	0,005	0,020	0,010	0,020
Physical therapist	0,029	0,033	0,097	0,031	0,097
Clinical health officer	0,014	0,016	0,038	0,015	0,038

Drug and supply unit cost

The cost of the dementia interventions primarily focuses on the drug costs, however costing of the full intervention is disaggregated into human resource costs, and drugs/supply costs. Costing for drugs is split up in costs for cholinesterase inhibitors, SSRIs and antipsychotics. Cholinesterase inhibitors are the golden standard. Antipsychotics should only be considered if there are no other alternatives to treat behavioral symptoms of dementia.

Table 6: Drug/supply component for dementia treatment

Drug/Supply	Number of units	Times per day	Days per case	Units per case	Price per pill (in US\$)	Cost per case (in US\$)
Cholinesterase inhibitors	1	1	365	1	1,7	620,5
SSRI	1	1	365	1	0,0096	3,5
Antipsychotics	1	1	42	1	0,0157	0,66

*Estimated from MSH price guide

Table 7: Total unit costs LIC/LMIC

	Total HR Costs LIC(in US\$)	Total HR Costs LMIC (in US\$)	Total drug costs (in US\$)	Other costs	Total costs LIC (in US\$)	Total costs LMIC (in US\$)
Diagnosis	2,05	5,87	n/a		2,05	5,87
Drug treatment (Cholinesterase inhibitors)	3,65	10,34	620,5		624,15	630,84
Drug treatment (SSRIs)	3,65	10,34	3,5		7,16	13,85
Drug treatment (antipsychotics)	3,65	10,34	0,66		4,31	11,0
Caregivers of dementia patients	0,43	0,9	n/a		0,43	0,9

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Appendix

Literature Review for effectiveness & safety

This was an unsystematic literature search and evidence range from Level 1 to level 3.

Level of evidence of efficacy studies:

1. low (expert opinions, case series, reports, low-quality case control studies)
2. moderate (high quality case control studies, low quality cohort studies)
3. high (high quality cohort studies, individual RCTs)
4. very high (multiple RCTs, metaanalysis, systematic review, clinical practice guidelines)