### ADDICTIONS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
<th>Study Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis Addiction(1)</td>
<td>1200mg twice daily</td>
<td>8 weeks</td>
<td>Randomised double-blind placebo-controlled trial</td>
<td>When drug tested, participants who received NAC had a twofold increase in likelihood of a negative urine cannabinoid test during treatment. NAC was well tolerated with minimal adverse effects.</td>
</tr>
<tr>
<td>Cocaine Addiction(2)</td>
<td>2400mg/day split over 4 doses</td>
<td>3 days</td>
<td>Double-blind placebo-controlled trial</td>
<td>The cocaine-dependent participants who received NAC had a reduced overall interest in cocaine in response to pictorial slides as well as a reduced desire to use cocaine.</td>
</tr>
<tr>
<td>Nicotine Addiction(3)</td>
<td>1200mg/day</td>
<td>6 months</td>
<td>Double-blind placebo-controlled trial</td>
<td>Participants who received NAC showed decreased markers of DNA damage compared to the placebo group, demonstrating a decrease in oxidative stress.</td>
</tr>
<tr>
<td>Nicotine Addiction(4)</td>
<td>1800mg twice daily</td>
<td>3.5 days</td>
<td>Double-blind placebo-controlled trial</td>
<td>Significant benefit seen in NAC group vs placebo group on Fagerstrom Test for nicotine dependence and measures of problem gambling severity.</td>
</tr>
<tr>
<td>Nicotine-Dependent Pathological Gambling(5)</td>
<td>1200-3000mg/day</td>
<td>12 weeks</td>
<td>Randomised double-blind placebo-controlled trial</td>
<td>16 out of 29 participants who suffered from confirmed pathological addiction to gambling who also received NAC experienced significant reductions in gambling behaviour over the trial period.</td>
</tr>
<tr>
<td>Pathological Gambling(6)</td>
<td>1800mg/day</td>
<td>6 weeks</td>
<td>Open-label double-blind placebo-controlled randomised trial</td>
<td>A complete abstinence from nail biting and related symptoms was observed among all of the patients. NAC’s beneficial effect was observed to continue even after the cessation of treatment.</td>
</tr>
</tbody>
</table>

### BEHAVIOURAL CONCERNS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
<th>Study Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nail Biting(7)</td>
<td>1000mg twice daily</td>
<td>24 weeks</td>
<td>Case report</td>
<td>A complete abstinence from nail biting and related symptoms was observed among all of the patients. NAC’s beneficial effect was observed to continue even after the cessation of treatment.</td>
</tr>
<tr>
<td>Skin Picking(8)</td>
<td>1200mg-2400mg/day</td>
<td>12 weeks</td>
<td>Double-blind placebo-controlled trial</td>
<td>The participants who received NAC had both a reduced urge to pick, as well as a reduction in the act of skin picking over the treatment period.</td>
</tr>
<tr>
<td>Trichotillomania (TTM) Adult(9)</td>
<td>1200mg-2400mg/day</td>
<td>12 weeks</td>
<td>Double-blind placebo-controlled trial</td>
<td>The participants who received NAC had a significantly greater reduction in hair-pulling symptoms as measured by 40-item NHP, PST, and CGI severity scales than those who received placebo.</td>
</tr>
<tr>
<td>Noise-Induced Hearing Loss (NIHL)(10)</td>
<td>1200mg/day</td>
<td>2 weeks</td>
<td>Randomised placebo-controlled clinical trial</td>
<td>Significant reduction in noise-induced temporary threshold shift in workers exposed to occupational noise.</td>
</tr>
</tbody>
</table>

### CARDIOMETABOLIC HEALTH

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
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<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperinsulinemia(11)</td>
<td>1800-3000mg/day</td>
<td>5-6 weeks</td>
<td>Randomised placebo-controlled trial</td>
<td>Improvement in circulating levels of insulin and peripheral insulin sensitivity.</td>
</tr>
<tr>
<td>Hyperhomocysteinaemia(12)</td>
<td>600mg/day</td>
<td>8 weeks</td>
<td>Randomised controlled trial</td>
<td>In patients with hyperhomocysteinaemia coronary artery disease, NAC lowered plasma homocysteine levels and improved endothelial function.</td>
</tr>
<tr>
<td>Hypertension(13)</td>
<td>600mg 3 times/day and ACE inhibitor or ACE inhibitor alone</td>
<td>21 days</td>
<td>Controlled crossover trial</td>
<td>The participants who received both NAC and the ACE inhibitor had significant reductions in both systolic and diastolic blood pressure.</td>
</tr>
<tr>
<td>Non-Insulin Dependent Diabetes(14)</td>
<td>1200mg/day</td>
<td>4 weeks</td>
<td>Randomised cross-over double-blind crossover trial</td>
<td>The participants who received NAC showed a decrease in plasma vascular cell adhesion molecule (VCAM) and intracellular GSSG, with an increase in both the GSH concentration and overall in the GSH/GSSG ratio. These results showed promise in showing the progression of vascular damage.</td>
</tr>
</tbody>
</table>

### MENTAL HEALTH

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
<th>Study Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD(15)(in patients with SLE)</td>
<td>2400-4800mg/day</td>
<td>3 months</td>
<td>Randomised double-blind placebo-controlled trial</td>
<td>Clinically significant symptom reduction of ADHD was observed in the NAC treatment group. Reporting completed in accordance to the ADHD self-report scale.</td>
</tr>
<tr>
<td>Alzheimer’s Disease(16)</td>
<td>500mg/kg/day</td>
<td>24 weeks</td>
<td>Double-blind placebo-controlled trial</td>
<td>Improved cognitive performance was observed in those who received NAC, with no change in peripheral measures of oxidative stress.</td>
</tr>
<tr>
<td>Autism(17)</td>
<td>900-2700mg/day</td>
<td>12 weeks</td>
<td>Double-blind randomised placebo-controlled trial on children aged 5-12</td>
<td>Results showed significant improvements on the Aberrant Behaviour Checklist (ABC) irritability subscale in particular in symptoms such as irritability, stereotypic behaviour, inappropriate speech and lethargy/social withdrawing. The dose was well-tolerated with limited side effects in irritability and hyperactivity/noncompliance.</td>
</tr>
<tr>
<td>Bipolar Disorder(18)</td>
<td>600mg-900mg/day</td>
<td>10 weeks</td>
<td>Randomised, double-blind placebo-controlled parallel trial</td>
<td>By week 10, the NAC group showed significantly more reduction in irritability and hyperactivity/noncompliance.</td>
</tr>
<tr>
<td>Depression(19)</td>
<td>1000mg twice daily</td>
<td>16 weeks</td>
<td>Randomised double-blind multi-centre placebo-controlled trial</td>
<td>A significant improvement seen in those with more severe depression in the middle tertile group. Significant rate of reduction of symptom severity from baseline to endpoint.</td>
</tr>
<tr>
<td>Mania(20)</td>
<td>1000mg twice daily</td>
<td>24 weeks</td>
<td>Placebo-controlled randomised trial</td>
<td>Improvement seen in manic symptoms in Young Mania Rating Scale scores while depressive symptoms worsened in the placebo group.</td>
</tr>
<tr>
<td>Obsessive Compulsive Disorder(21)</td>
<td>600-2400mg/day</td>
<td>12 weeks</td>
<td>Randomised double-blind placebo-controlled trial</td>
<td>Treatment group showed a significantly improved Yale-Brown Obsessive Compulsive Scale score. 52% of which were full responders by the study endpoint.</td>
</tr>
<tr>
<td>Parkinson’s Disease (PD)(22)</td>
<td>600mg twice daily</td>
<td>3 months</td>
<td>Randomised, placebo-controlled trial</td>
<td>The PD group treated with NAC showed a significant increase (up to 8%) dopamine transporter binding, a mean improvement of 12.9% on the Unified Parkinson’s Disease Rating Scale and significant changes in the midbrain serotonin transporter binding.</td>
</tr>
<tr>
<td>Schizophrenia(23)</td>
<td>1000mg twice daily</td>
<td>24 weeks</td>
<td>Randomised double-blind multi-centre placebo-controlled trial</td>
<td>A significant improvement was observed in negative symptoms based on the Positive and Negative Symptoms Scale (PANSS). These improvements were reviewed within one month of stopping the NAC.</td>
</tr>
<tr>
<td>Traumatic Brain Injury(24)</td>
<td>1500-2000mg/day</td>
<td>1 week</td>
<td>Randomised double-blind placebo-controlled study</td>
<td>NAC group showed a complete resolution of mild traumatic brain injury symptoms, such as headaches, hearing loss and neurocognitive dysfunction.</td>
</tr>
</tbody>
</table>

### HEPATIC/RENAI HEALTH

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
<th>Study Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Alcoholic Fatty Liver Disease (NAFLD)(25)</td>
<td>600mg/12 hours</td>
<td>12 weeks</td>
<td>Comparative study</td>
<td>After three months of treatment, participants who received NAC had significantly lower levels of serum alanine aminotransferase. This effect was found to be independent of the grade of steatosis prior to the intervention. NAC was also found to significantly reduce the span of the spleen.</td>
</tr>
<tr>
<td>Non-Alcoholic Steatohepatitis (NASH)(26)</td>
<td>1200mg/day + metformin</td>
<td>52 weeks</td>
<td>Comparative study</td>
<td>This study showed that serum alanine aminotransferase, high-density lipoproteins, insulin, glucose concentrations and the homocysteine model assessment (HOMA) index were significantly reduced at the end of study. NAC was also observed to decrease liver steatosis and fibrosis.</td>
</tr>
<tr>
<td>Endothelial Dysfunction (ED) – Chronic Kidney Disease(27)</td>
<td>600mg twice daily</td>
<td>6 weeks</td>
<td>Controlled clinical trial</td>
<td>Compared to controls, those on haemodialysis were found to have reduced flow-mediated dilatation – a measure of vasodilation. NAC was found to prevent the reduction in flow-mediated dilatation, suggesting that NAC treatment could improve ED.</td>
</tr>
<tr>
<td>Cardiorenal Syndrome(28)</td>
<td>500mg twice daily</td>
<td>4 weeks</td>
<td>Double-blind placebo-controlled trial</td>
<td>An improvement in endothelial function, and forearm blood flow in the NAC treatment group was observed compared to the placebo group.</td>
</tr>
<tr>
<td>Nephropathic Cystinosis(29)</td>
<td>25mg/kg/day</td>
<td>3 months</td>
<td>Controlled clinical trial</td>
<td>Renal function was significantly improved and oxidative stress reduction was seen in the NAC treatment group.</td>
</tr>
</tbody>
</table>
**Clinical Application**

**N-Acetylcysteine**

### IMMUNE

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Allergic Rhinitis**(a)**</td>
<td>50mg-250mg/kg/day</td>
<td>-</td>
<td>In vitro studies</td>
<td>NAC significantly inhibited the accumulation of inflammatory cells down-regulated inflammatory molecules such as TNFα and decreased the expression of COX-2. The findings suggest that NAC may be able to suppress the allergens induced nasal inflammatory cascade.</td>
</tr>
<tr>
<td>Helicobacter Pylori Infection**(b)**</td>
<td>400mg three times daily + Clarithromycin and Lansoprazole</td>
<td>10 days</td>
<td>Controlled clinical trial</td>
<td>NAC was observed to have an additive effect on the eradication rates of H. pylori obtained with dual therapy using Lansoprazole and Clarithromycin. The authors suggest that NAC may have improved the delivery of the antibiotics at the site of infection due to its ability to reduce the thickness of the mucosa.</td>
</tr>
<tr>
<td>Human Immunodeficiency Virus (HIV)<strong>(c)</strong></td>
<td>1000mg daily</td>
<td>52 weeks</td>
<td>Randomized placebo-controlled trial</td>
<td>Participants suffering from HIV infection who received NAC had increased levels of sulfur containing amino acids and GSH while the control group who received placebo had equalised taurine and GSH levels.</td>
</tr>
<tr>
<td>Influenza**(d)**</td>
<td>600mg twice daily</td>
<td>24 weeks</td>
<td>Controlled randomised and double-blind model</td>
<td>NAC treatment was well tolerated and resulted in a significant decrease in the frequency of influenza-like episodes, severity and length of time confined to bed. Both local and systemic symptoms were significantly reduced in the NAC group - in particular the elderly high-risk group.</td>
</tr>
<tr>
<td>Sjögren’s Syndrome**(c)**</td>
<td>200mg three times daily</td>
<td>4 weeks</td>
<td>Double-blind crossover trial</td>
<td>NAC was shown to improve ocular symptoms and irritability, as well as halitosis and dry eye. The authors suggest that NAC may have improved keratoconjunctivitis sicca.</td>
</tr>
<tr>
<td>Systemic Lupus Erythematosus (SLE)<strong>(c)</strong></td>
<td>600mg-2400mg twice daily</td>
<td>12 weeks</td>
<td>Double-blind placebo-controlled phase II trial</td>
<td>NAC increased GSH in peripheral lymphocytes and improved disease activity in SLE patients. The authors suggest that NAC may be able to safely improve lupus disease activity by blocking ROS in SLE lymphocytes.</td>
</tr>
</tbody>
</table>

### TOXICITIES

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
<th>Study Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy Adverse Effects**(e)**</td>
<td>1200mg/day</td>
<td>12 treatment cycles</td>
<td>Randomised controlled trial</td>
<td>NAC was found to reduce the incidence of oxalate-induced nephropathy in renal cancer patients receiving oxalate-based adjuvant chemotherapy.</td>
</tr>
<tr>
<td>Heavy Metals**(c)**</td>
<td>200-400mg daily or twice daily</td>
<td>12 weeks</td>
<td>Randomised controlled trial</td>
<td>Compared to their baseline data, the participants who received NAC had significantly lower urinary lead levels. NAC decreased oxidative stress in workers exposed to lead through stimulating GSH synthesis.</td>
</tr>
</tbody>
</table>

### FERTILITY AND REPRODUCTION

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
<th>Study Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometriosis**(f)**</td>
<td>600mg three times daily for 5 days/ week</td>
<td>12 weeks</td>
<td>Observation cohort study</td>
<td>NAC was found to both prevent the growth of cysts as well as reduce the size of existing cysts. 50% (24 patients) of the NAC treated group cancelled their scheduled laparoscopic surgery due to either decreased or disappeared cysts, pain reduction or pregnancy.</td>
</tr>
<tr>
<td>Female Infertility**(c)**</td>
<td>1200mg NAC + 50mg Clomiphene citrate twice daily</td>
<td>2 months</td>
<td>Prospective cross-over trial</td>
<td>NAC was shown to improve ovarian function, to increase ovulation rates and reduce frequency of spontaneous abortion. 50% of the patients with infertility who received NAC had equalised taurine and GSH levels.</td>
</tr>
<tr>
<td>Male Infertility**(c)**</td>
<td>600mg/day + 200mg sodium bicarbonate</td>
<td>26 weeks</td>
<td>Double-blind placebo-controlled randomised trial</td>
<td>The participants who received NAC were observed to have improvements in all semen parameters. A reduction in follicle-stimulating hormone (FSH) and an increase in seminal volume and sperm concentration were observed, as well as an overall improvement in semen quality.</td>
</tr>
<tr>
<td>Miscarriage Prevention**(g)**</td>
<td>600mg/day + 500µg folic acid</td>
<td>Up to 20 weeks gestation</td>
<td>Controlled clinical trial</td>
<td>Compared with folic acid alone, NAC + folic acid was also observed as an overall improvement in semen quality.</td>
</tr>
<tr>
<td>PCOS**(h)**</td>
<td>600mg three times daily</td>
<td>24 weeks</td>
<td>Randomised, double-blind clinical trial</td>
<td>In comparison to Metformin (500mg three times daily), the NAC group showed more statistically significant improvement according to Body Mass Index, fasting blood sugar, HOMA index and LDL.</td>
</tr>
<tr>
<td>Polycystic Ovarian Syndrome (PCOS)<strong>(i)</strong></td>
<td>1800 or 3000mg/day</td>
<td>5-6 weeks</td>
<td>Randomised placebo-controlled trial</td>
<td>Compared to baseline data, decreases were observed in the hormone scores, body mass index and HOMA index, and improvements were seen in insulin sensitivity, menstrual irregularity and free testosterone.</td>
</tr>
<tr>
<td>Preeclampsia**(j)**</td>
<td>400mg/day + 250mg methyldopa</td>
<td>6 weeks</td>
<td>Controlled clinical trial</td>
<td>Improved both weight gain and appetite, proteinuria, activity and respiration scores were observed among mothers treated with NAC. NAC ameliorated the severity of oxidative stress in preeclampsia but did not alter the disease itself.</td>
</tr>
<tr>
<td>Pregnancy Support**(k)**</td>
<td>600mg/day + plus 17 Hydroxyprogesteroneone caprate</td>
<td>Until 36 weeks of pregnancy or active labor</td>
<td>Randomised, double-blind, placebo-controlled trial</td>
<td>Oral NAC was found to reduce the recurrence of preterm birth in patients with bladder vaginos. More of the patients in the NAC group reached 36 weeks of pregnancy than in the placebo group. The gestational age at delivery was also significantly higher in the NAC group than in the placebo group.</td>
</tr>
</tbody>
</table>

### RESPIRATORY

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Bronchiolitis**(l)**</td>
<td>1800mg/day</td>
<td>16 weeks</td>
<td>Double-blind model</td>
<td>NAC was observed to shorten the duration of asthmatic inflammation of the throat and cough as well as reduce overall symptomatology and pulmonary air flow values to normal in patients with either simple or recurrent catarrhal bronchitis after 4 days of treatment.</td>
</tr>
<tr>
<td>Chronic Bronchitis**(m)**</td>
<td>200-600mg twice daily</td>
<td>24 weeks</td>
<td>Placebo-controlled double-blind parallel group study</td>
<td>The exacerbation rate was significantly lower in those who received NAC - with 40% of the patients remaining free from exacerbations compared to 19% who received placebo.</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary Disease (COPD)<strong>(n)</strong></td>
<td>400mg three times daily</td>
<td>10 days</td>
<td>Randomized controlled double-blind study</td>
<td>NAC treatment significantly decreased sputum MDA and IL-8 levels and improved sputum pulmonary function tests.</td>
</tr>
<tr>
<td>Cystic Fibrosis**(o)**</td>
<td>600mg 1000mg three times daily</td>
<td>4 weeks</td>
<td>Phase 1 study</td>
<td>NAC was seen to relieve the inflammatory and n哆 imbalance commonly seen in Cystic Fibrosis.</td>
</tr>
<tr>
<td>Obstructive Sleep Apnoea**(p)**</td>
<td>600mg three times daily</td>
<td>4 weeks</td>
<td>Randomised placebo-controlled trial</td>
<td>A significant improvement in sleep/postracheal parameters, oxygen characteristics and beneficial effects on oxygen saturation were observed. Based on these findings, the authors suggest that NAC may also reduce dependency on continuous positive airway pressure therapy.</td>
</tr>
<tr>
<td>Smoking**(q)**</td>
<td>600mg/day</td>
<td>8 weeks</td>
<td>Comparative study</td>
<td>NAC administration increased lymphocyte concentration, phagocytic activity of alveolar macrophages and the secretion of leukotrienes. These effects stopped when NAC was discontinued.</td>
</tr>
</tbody>
</table>

### SPORTS NUTRITION

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Performance**(r)**</td>
<td>600mg twice daily</td>
<td>9 days</td>
<td>Double-blind randomised placebo-controlled trial</td>
<td>The treatment group had an improvement in sprint performance during cycling performance via promoting adaptive processes and improvements in n哆 balance.</td>
</tr>
<tr>
<td>Respiratory Muscle Fatigue**(s)**</td>
<td>1800mg 45-60 min prior to exercise test</td>
<td>2-4 sessions within 1 week</td>
<td>Placebo-controlled trial</td>
<td>Acute doses of NAC reduce respiratory muscle fatigue during heavy exercise.</td>
</tr>
<tr>
<td>High-Intensity Interval Exercise (HIIE)<strong>(t)</strong></td>
<td>1000mg/kg with glucose</td>
<td>6 x 5 minute HIIE bouts at 82% power output</td>
<td>2 x Double-blind repeated measures crossover trial</td>
<td>NAC decreased mean power output and altered substrate metabolism and muscle fibre type recruitment during the exercise, which is vital to time-trial performance.</td>
</tr>
<tr>
<td>Overall Athletic Performance**(u)**</td>
<td>600mg twice daily</td>
<td>1 week</td>
<td>Randomised placebo-controlled trial</td>
<td>Controlled lactate production, maintained total antioxidant capacity, maximised oxygen uptake and improved muscle fatigue was seen in the treatment group.</td>
</tr>
</tbody>
</table>

### CHILDREN’S RESPIRATORY

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Duration</th>
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<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Respiratory Tract Infections**(v)**</td>
<td>100-300mg/day + anti-bacterial agent</td>
<td>6 days</td>
<td>Controlled trial</td>
<td>Fever, cough, dyspnoea and thoracic: most rates returned to normal in a significantly shorter time with NAC than with placebo.</td>
</tr>
<tr>
<td>Bronchiitis**(w)**</td>
<td>100-200mg three times daily</td>
<td>4 days</td>
<td>Controlled trial</td>
<td>NAC was observed to shorten the duration of asthmatic inflammation of the throat and cough as well as reduce overall symptomatology and pulmonary air flow values to normal in patients with either simple or recurrent catarrhal bronchitis after 4 days of treatment.</td>
</tr>
<tr>
<td>Obstructive Bronchial Diseases**(y)**</td>
<td>10-30mg/kg twice daily or three times daily</td>
<td>7-11 days</td>
<td>Mean=2.9 yrs (mean=36 days)</td>
<td>Controlled trial</td>
</tr>
</tbody>
</table>